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MACROSOMIA, CARDIAC HYPERTROPHY, ERYTHROBLASTOSIS, AND HYPERPLASIA OF THE ISLANDS OF LANGERHANS IN INFANTS BORN TO DIABETIC MOTHERS

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INTRODUCTION

THE only anatomical variants that have been generally recognized in infants born of diabetic mothers are excessive body weight and increase in the size and number of the islands of Langerhans. Their exact incidence is not known, but it is significantly greater than in the normal newborn infant population. In the present communication it will be shown that other important deviations from the normal anatomy of the newborn infant are to be found in some infants born to diabetic mothers; namely, a marked hypertrophy of the heart and an increase in the erythropoietic tissue of the liver. In fact, we have observed that macrosomia, hyperplasia of the islands of Langerhans, cardiac hypertrophy, and erythroblastosis occur together in the same infant in a surprising number of cases.

Our attention was directed to these findings by a recent study made in this clinic of six infants born to diabetic mothers.[1] Two of the infants had by roentgen examination considerable enlargement of their hearts in the first few days of life. Similar observations have been made here in four additional infants. The observations in these ten infants led us to search the literature and the autopsy files of the New Haven Hospital, the New York Hospital,* and the Boston Lying-In Hospital† for anatomical confirmation of the roentgen evidence of

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cardiac enlargement. This report summarizes the clinical and roentgen studies on the ten infants referred to above and presents the results of the post-mortem investigations on eighteen other infants.

TECHNIQUE AND METHODS

The roentgenographic examinations of the chests were all made with a target film distance of six feet. The routine posteroanterior and left lateral views were often supplemented with supine anteroposterior views to minimize the error due to the variations in the height of the diaphragm. Cardiac mensuration was carried out in both the frontal and lateral views. In selecting films for measurement the degree of respiratory expansion as indicated by the height of the diaphragm and the transverse thoracic diameter was taken into account. The greatest transverse diameter of the heart was taken as the sum of the right and left median transverse diameters. The anteroposterior cardiac diameter was measured from the lateral views. The transverse diameter of the thorax was measured at the level of the diaphragm. The relation of the left dome of the diaphragm to the posterior ribs was recorded. The roentgen studies were repeated frequently in most instances during the first two weeks of life and follow-up examinations were carried out over a period of months wherever possible. A group of eight normal infants served as controls. The control group was selected so that each normal infant would correspond in birth weight, sex, and body length to one of the infants in the "diabetic" group. The roentgen studies were made in the control group on the same day of life as for the corresponding infant in the "diabetic" group and were limited to the first ten days of life.

The infants in the normal and "diabetic" groups were cared for on the pediatric service throughout their stay in the hospital. All of the infants have come under the personal observation of one of us (H. C. M.).

Blood sugar concentrations were determined at frequent intervals during the first few days of life by the Shaffer-Hartmann method or by the micromethod previously described.[1]

The post-mortem diagnoses were accepted as stated in the protocols.

RESULTS

Table I shows the clinical and roentgen findings in ten babies born to diabetic mothers in the New Haven Hospital since 1936. Cases 1 to 6 have been previously reported.[1] Brief histories on the new cases (Cases 7 to 10) are given at the end of this report. The age of the infant at which each roentgen examination was made and the results are shown in the column "Roentgen Diagnosis." The diagnosis of an enlarged heart was based on the comparison of the greatest transverse diameter of the heart to that of the thorax. A cardiothoracic ratio of 55 or greater was arbitrarily accepted as evidence of cardiac enlarge-

ment. This was justified by the fact that in the control group ratios greater than 55 were encountered in only four of the seventeen examinations, whereas in the "diabetic group" ratios greater than 55 were observed in twenty of the twenty-one examinations made in the first ten days of life. It is observed that there is a definite trend of the heart to become progressively smaller. Cardiothoracic ratios greater than 65 are seen only in the first ten days of life, and by the end of the first six weeks of life the hearts of all infants with follow-up examinations

TABLE I

RELATION OF SYMPTOMS TO ROENTGEN EVIDENCE OF CARDIAC ENLARGEMENT AMONG INFANTS OF DIABETIC MOTHERS

CASE	UNIT NO.	BIRTH WEIGHT (GM.)	SYMPTOMS AND DAY	ROENTGEN DIAGNOSIS		
				DAY	MONTH	YEAR
1	A75948	4,720	None	1, E		
2	A76445	3,650	None	1, E; 10, N		
3	A78473	3,545	None	7, E		
4	A68553	4,580	Dyspnea, 1	1, E; 3, E; 7, E		?, N
5	A76059	2,650	Cyanosis, 1 Convulsions, 10	2, ME	1, N	1¾, N
6	A68045	3,710	Marked cyanosis, 1, 4, 5, 6, 7, 8	4, ME; 7, ME; 10, ME; 16, E	3½, N	
7	B9835	4,320	Moderate cyanosis, 1, 2	3, ME; 8, E; 11, E; 21, E	5½, N; 10, N	
8	B11908	3,425	Shock, 1 Cyanosis, 1, 2	1, ME; 2, E; 4, E; 8, E; 15, E	2, N; 4½, N; 8, N	1½, N
9	B32972	3,280	Marked cyanosis, 1, 2, 3, 4, 5, 6 Dyspnea, 1, 2	1, ME; 10, E		
10	B33765	3,720	Cyanosis and dyspnea, 1-12	1, E; 4, E; 11, E	1½, E	

N, Normal; E, enlargement; ME, marked enlargement.

$\frac{\text{Diameter of heart}}{\text{Diameter of thorax}}$ = 54 or less, N; 55 to 64, E; 65 or more, ME.

had returned to normal size. Seven of the ten infants (Cases 4 to 10) had symptoms, as indicated in Table I. The period of symptoms corresponds with the period during which marked enlargement of the hearts was noted in the roentgenograms. Cyanosis was the most common finding. It was present in six infants, three of whom required the use of an oxygen tent for several days. In none of the infants could any direct correlation be made out between the symptoms or clinical course and the concentration of the blood sugar. This lack of correlation has been noted previously by Miller and Ross.[1] A comparison of the severity of the mothers' diabetes and complications of pregnancy with the clinical courses and roentgen findings in the infants failed to reveal any clear-cut relationship. The diabetes was uniformly well regulated throughout the pregnancies of the mothers.

The progressive decrease in cardiothoracic ratios is illustrated in the patient in Case 8, Figs. 1 to 4. In this instance there was little change in the transverse cardiac diameter in the first week of life.

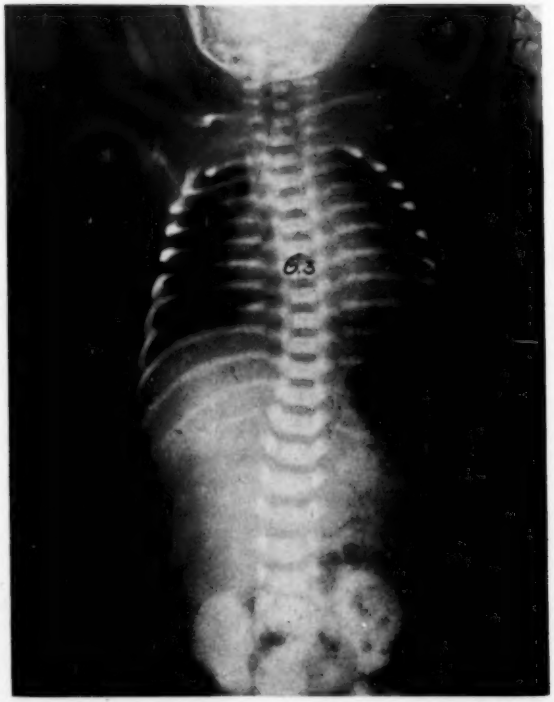

Fig. 1 (Case 8).—First day of life; transverse thoracic diameter, 9.7 cm.; transverse cardiac diameter, 6.3 cm.

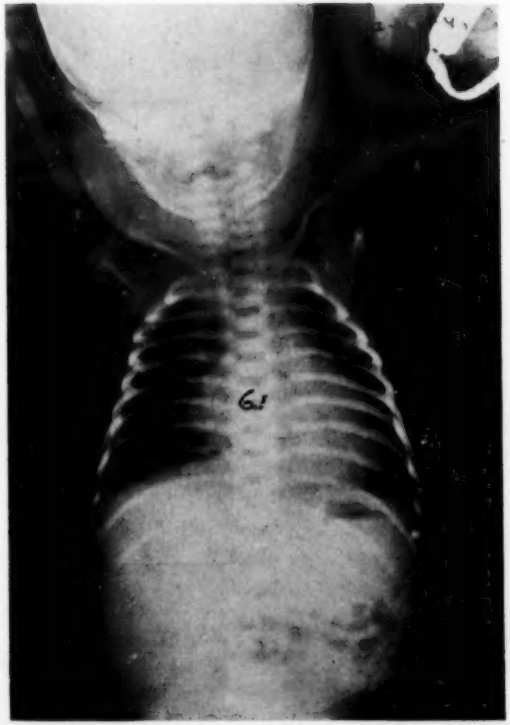

Fig. 2 (Case 8).—Eighth day of life; transverse thoracic diameter, 10.1 cm.; transverse cardiac diameter, 6.1 cm.

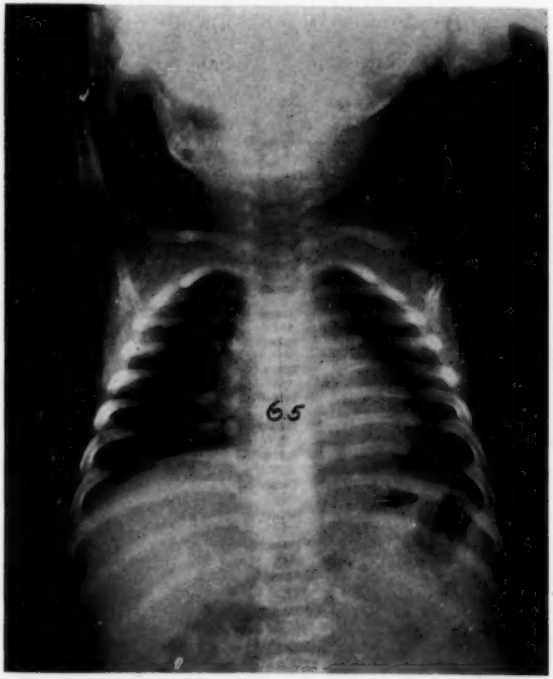

Fig. 3 (Case 8).—Two months of age; transverse thoracic diameter, 12.5 cm.; transverse cardiac diameter, 6.5 cm.

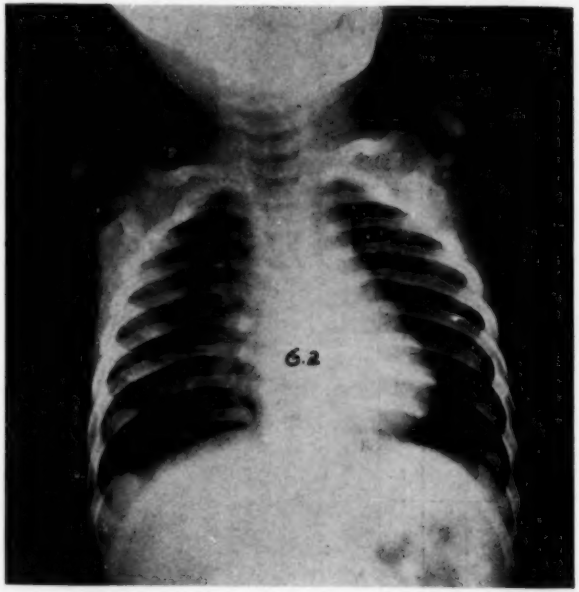

Fig. 4 (Case 8).—Four and one-half months of age; transverse thoracic diameter, 13.2 cm.; transverse cardiac diameter, 6.2 cm.

TABLE II

X-RAY MEASUREMENTS OF HEARTS AND CHESTS

GROUP	NUMBER OF PATIENTS	X-RAYS	TRANS. DIAM. OF HEART (CM.)	TRANS. DIAM. OF CHEST (CM.)	RIB LEVEL OF DIAPHRAGM
Normal	8	17	4.85 ±0.13	9.51 ±0.07	7.56 ±0.29
"Diabetic"	8	17	6.21 ±0.25	9.53 ±0.22	8.44 ±0.19

±, Standard error.

The cardiac and thoracic measurements for the eight control infants and for eight of the ten infants from Table I are shown in Table II. The data on Cases 1 and 3 in Table I were omitted from Table II, since but one roentgen examination had been made in each infant. The average transverse diameter of the hearts of the infants in the "diabetic" group was 6.21 cm. and in the normal infants, 4.85 cm. The difference is statistically highly significant. It was noted that the level of the diaphragm averaged one interspace lower in the infants in the "diabetic" group than in those in the normal group. The greater descent of the diaphragm in the "diabetic" infants would, if anything, tend to make the transverse diameters of their hearts smaller, thus increasing the significance of the difference in the cardiac diameters between the two groups. No significant difference was noted in the average anteroposterior diameters of the hearts in the lateral views in the two groups, and hence they were not included in Table II.

The evidence of cardiac hypertrophy as obtained from the eighteen infants in whom the hearts had been weighed in the post-mortem study is summarized in Table III. Brief histories on the four infants born in the New Haven Hospital (Cases 7, 8, 9, and 16) are given at the end of this report. With the exception of Cases 8 and 9, the mothers of the infants listed in Table III were known diabetics prior to either conception or delivery. In Cases 8 and 9 the mothers developed diabetes subsequent to the delivery of these infants. At the time of their confinement both mothers had fasting blood sugars of 75 and 68 mg. per cent, respectively, and examination of their urine during the postpartum period showed them to be free of reducing substances. Cases 8 and 9 have been included in Table III because the anatomical findings of these infants were similar to those observed in the infants whose mothers had diabetes prior to delivery.

The infants whose cases are given in Table III may be conveniently divided into two groups, those who weighed over 3,900 Gm. at birth and those who weighed less. In the first group are nine infants (Cases 1 to 9), all but one of whom (Case 9) had hearts which weighed over 29 Gm. Scammon states that the absolute values for cardiac weight in newborn infants are between 20 and 25 Gm.[5] Thus, the eight infants in the first group whose hearts weighed over 29 Gm. may be considered as

TABLE III

POST-MORTEM OBSERVATIONS IN BABIES BORN TO MOTHERS WITH DIABETES MELLITUS

CASE	TIME OF DEATH	BIRTH WEIGHT (GM.)	HEART WEIGHT (GM.)	HYPERPLASIA ISLANDS OF LANGERHANS	HEMOPOIESIS IN LIVER	SOURCE
1	Stillborn	3,920	35	Present	Moderate	Hurwitz and Irving[2]
2	72 hr.	3,930	38	Present	--	Helwig[4]
3	72 hr.	4,500	40	Present	?	New York Hospital
4	48 hr.	4,000	70	Marked	Increased	New York Hospital
5	59 hr.	3,930	38	?	Many areas	Boston Lying-In Hospital
6	Stillborn	4,310	34	?	Numerous areas	Boston Lying-In Hospital
7	Stillborn	5,070	49	Present	Increased	New Haven Hospital
8*	Stillborn	5,490	65	Present	?	New Haven Hospital
9*	Stillborn	5,850	29	--	Increased	New Haven Hospital
10	15 hr.	3,870	26	Marked	Marked	Boston Lying-In Hospital
11	47 hr.	3,310	32	Considerable	No	Boston Lying-In Hospital
12	13 hr.	2,780	27	Present	Increased	Smyth and Olney[3]
13	Stillborn	3,080	24	No	No	New York Hospital
14	48 hr.	2,980	20	No	No	New York Hospital
15	Stillborn	2,880	18	No	No	Boston Lying-In Hospital
16	13 days	2,290	19	No	No	New Haven Hospital
17	24 hr.	2,270	21	Present	No	New York Hospital
18	24 hr.	2,200	17	No	No	New York Hospital

*Mothers developed diabetes mellitus subsequent to the delivery of these fetuses.

having abnormally heavy hearts. In Cases 3 and 7 the hearts of the infants weighed twice as much as normally expected, and in Cases 4 and 8 the increments were three times the expected weight. Among the nine infants (Cases 10 to 18) who weighed less than 3,900 Gm. at birth, there was only one infant (Case 11) who had a heart that weighed more than 29 Gm. Two others (Cases 10 and 12) had hearts weighing more than 25 Gm., the upper limit of normal as given by Scammon, but less than 29 Gm. Unpublished work in this clinic on the weights of hearts of normal infants whose birth weight was over 2,500 Gm. indicates that the limits of weight of the normal heart as given by Scammon are too close and that variations from 16 to 29 Gm. may be expected.[6]

Hyperplasia of the islands of Langerhans was noted in ten of the eighteen infants in the cases in Table III. Six of the nine infants with a birth weight of 3,900 Gm. or more (Cases 1, 2, 3, 4, 7, and 8) and four of the nine with birth weights less than 3,900 Gm. (Cases 10, 11, 12, and 17) were found to have hyperplastic islets in the pancreas. The diagnosis of hyperplasia of islet tissue was based on an inspection of the microscopic sections and not on any systematic measurements of the islands. Perhaps more careful study would have altered the results, but the changes in the islands were so notable that the diagnosis of hyperplasia seems reasonably certain.

Excessive amounts of hemopoietic tissue were noted to be present in eight of the seventeen livers studied histologically. Six of the nine infants with birth weights over 3,900 Gm. (Cases 1, 4, 5, 6, 7, and 9) and two of the nine infants who weighed less than 3,900 Gm. at birth (Cases 10 and 12) had more than usual amounts of erythroblastic tis-

sue in the liver. Hemopoietic tissue was observed in the other viscera in some of the infants, but no other organ was found to have such pronounced amounts as observed in the liver, nor were the other organs involved so frequently.

An excessive body weight, cardiac hypertrophy, hyperplasia of the islands of Langerhans, and excessive amounts of hemopoietic tissue in the liver were found in combination in three of the infants whose cases appear in Table III (Cases 1, 4, and 7).

DISCUSSION

Mortality rates among infants whose mothers have diabetes mellitus are invariably high. The stillbirth rate is several times that found in the general population, and, if the infant is born alive, his chances for survival are greatly reduced. A gross mortality rate of about 30 per cent still exists in spite of the advent of insulin. Many theories have been advanced to explain the high death rate. Among the more prominent of these are the poor regulation of the maternal diabetes,[2, 10] the presence of toxemia of pregnancy in the mothers,[11, 12] hormonal imbalance in the mothers,[13] hypoglycemia in the infants,[14, 15] and the large size of the fetus.[2, 10, 16] There is no general agreement, however, as to the validity of any of the above theories. In fact, it has been claimed that the lack of control over the maternal diabetes is not a factor in the high stillbirth rate[12] and that the hypoglycemia is not per se the cause of neonatal death.[1, 7, 10] In the light of the anatomical findings reported here, the above theories will, of necessity, have to be modified. In seeking an explanation for the cause of death and the high morbidity, the possibility of a hypertrophied heart, hyperplasia of the islands of Langerhans, an excessive body weight, and erythroblastosis, as well as the infant's hypoglycemia and the state of the mother's health, will have to be kept in mind. Our data do not permit us to state categorically that death resulted from any one or a combination of these factors, since evidence has been presented in the roentgenograms to show that a marked enlargement of the heart may be present without a fatal consequence, and it is known that these infants can have large numbers of erythroblasts in the peripheral blood and marked hypoglycemia and survive.[1] The only clear-cut explanation of death is to be found in those infants with an excessive body weight where the dystocia undoubtedly was the lethal factor. In the present state of our knowledge we can recognize only that other anatomical variants besides macrosomia do exist in these infants and that they may have an important bearing on the course and survival of the infant. The theory that the control of the maternal diabetes during the period of gestation is a prime factor in the infant mortality deserves special consideration. Undoubtedly the fetus may be fatally affected by severe acidosis or hypoglycemic shocks in the mother. On the other hand, the

notion that the careful regulation of the mother's blood sugar concentration is the deciding factor in the infant's survival will have to be viewed with considerable skepticism in light of the fact that the same marked anatomical changes can occur in the fetuses of prediabetic mothers (Cases 8 and 9, Table III) as in those whose mothers have overt symptoms and signs of the disease. It is true that insulin has increased the fertility of women with diabetes and has greatly reduced the risk to them of child bearing, but there are no data to show that during the two decades insulin has been used there has been any appreciable change in the risk to the infant.

It is well known that the morbidity during the first few days of life is very high in infants born to diabetic mothers. Sisson's report on sixty-five liveborn infants of diabetic mothers especially brings out this point.[7] In the infants in his series as well as in the ten infants reported here in Table I, cyanosis was the outstanding finding with dyspnea and tachypnea next in frequency. Twitching and convulsions seldom occurred. The early theory that these findings were attributable to the hypoglycemia that was almost always present has not been supported by more recent critical examination.[1, 7, 10] Sisson concluded that the symptomatology was more likely the result of interference with respiration, either due to injury of the respiratory centers or to atelectasis, although little evidence was brought forward to support this theory.[7] The observations made here, that these infants may have considerable cardiac enlargement during the period when symptoms occur, suggest the possibility that the symptomatology may be cardiac in its origin. No conclusive proof of this possibility can be given at the present time, but the facts are striking enough to warrant further attention. Atelectasis as an explanation for the respiratory symptoms observed in the ten infants in our series was notable by its absence in the twenty-one roentgen examinations made in the ten infants during the first ten days of life. The fact that the symptoms in the infants in our series were almost entirely respiratory in character and the fact that the cyanosis cleared in every instance when oxygen was administered do not detract from the theory that they may have been cardiac in origin. Cases of so-called "idiopathic cardiac hypertrophy" in a somewhat older group of infants have as their outstanding features cyanosis, dyspnea, tachypnea, and restlessness, just as did the infants in this study and in other reported series. The clinical diagnosis in the cases of "idiopathic cardiac hypertrophy" is usually pneumonia, and the correct diagnosis is often made after the roentgenograms have been taken or at the autopsy table.

The explanation for the cardiac hypertrophy must await further studies. The observation of excess glycogen deposition in the myocardium made by Hurwitz and Irving[2] may be highly pertinent and should be followed up by chemical determinations of the glycogen in the myocardium of these infants whenever the opportunity presents

itself. Durlacher has recently observed four cases of erythroblastosis fetalis post mortem and found that there was not only marked cardiac enlargement, but also excessive depositions of glycogen in the myocardium.[9] The association of cardiac hypertrophy with erythroblastosis fetalis in infants of nondiabetic mothers strengthens the belief that the cause of the cardiac hypertrophy in the "diabetic" group may also be the result of excess glycogen deposition. Some other component in addition to an excess of glycogen must be present to account for the excessive weights of the hearts in the "diabetic" group. Whether the increased weight is wholly the result of an accumulation of interstitial fluid or an increase in all the cellular components will have to be determined by an analysis of wet and dry weights. The question arises whether or not the cardiac hypertrophy is simply dependent on the excessive body weight. This seems unlikely, since the heaviest of the infants reported in Table III would correspond in weight to a normal infant 2 or 3 months of age, and Copoletta and Wolbach[17] have shown that the average weight of the hearts of infants 2 to 3 months of age is 23 Gm., which is about one-half the weight of the hearts of the large infants whose cases appear in Table III. According to the latter authors, hearts of 40 Gm. would be expected in infants 1 year old and such infants would weigh approximately 10 kg.

No attempt has been made to give a complete report of the pathologic changes found at autopsy in this study, since we did not consider ourselves competent to make a complete evaluation. Certain gross and microscopic changes were recorded because they supported our clinical and roentgen observations and also because of their unusual incidence and relations one to another. Not the least striking feature of this pathologic material was the fact that macrosomia, cardiac hypertrophy, excessive hemopoiesis in the liver, and hyperplasia of the islands of Langerhans were found associated together in three of the eighteen infants examined post mortem. The significance of this observation is far from clear. The interest that attaches to it is considerably increased by the fact that these same anatomical findings have been found together in infants with erythroblastosis fetalis born to nondiabetic mothers. Potter, Seckel, and Stryker[18] have recently found that some of their infants who died with erythroblastosis fetalis had marked hyperplasia of the islands of Langerhans. Durlacher's observation that infants dying with erythroblastosis fetalis were found to have cardiac hypertrophy has already been noted. Hyperplasia of the islands of Langerhans, as well as massive edema, has also been seen by Durlacher in the infants in his cases. Whether or not the massive edema which characterizes many of the cases of erythroblastosis fetalis in infants who die is in any way comparable to the excessive body weight of the infants of diabetic mothers is not clear. Some of the latter infants have edema but nothing like the amount seen in infants with hydrops fetalis. The observation that this group of anatomical

variants is found under such divergent conditions suggested the possibility of some common factor as yet unknown in their etiology. The possibility of a Rh factor as a basis for the anatomical findings in the infants in the "diabetic" group was studied. Results of such tests made on several of the mothers with diabetes showed them all to be Rh positive.[20] The most recently born infant of a diabetic mother in the New Haven Hospital was found to have 60,000 nucleated red blood cells per cubic millimeter of blood on the first day of life, and a gradual diminution in the number of erythroblasts occurred during the next ten days. No anemia or jaundice of any note developed. The mother was Rh positive. The fact that the diabetic mothers appear to be like the general population in the distribution of the Rh factor does not preclude the possibility that some common factor may be operating to produce the similar anatomical changes seen in infants of diabetic mothers and in infants with erythroblastosis fetalis born to nondiabetic mothers, however dissimilar the two diseases may appear to be. It is well known that normablasts may be present in the liver and blood in conditions other than erythroblastosis fetalis, for example, syphilis and septicemia. It is also clear that the Rh factor does not explain all the cases of erythroblastosis fetalis. Thus, there is reason for considering other factors in its etiology. It is also necessary to consider other factors than hypo-insulinism and hyperglycemia in the diabetic mothers as explanations for the syndrome observed in their offspring, since these two factors were excluded in the infants in Cases 8 and 9 of Table III. The absence of a complete or satisfactory explanation for the pathologic changes observed either in infants of diabetic mothers or in infants with erythroblastosis fetalis will necessitate further study and research.

Appraisal of the data in Table III suggests that cardiac hypertrophy, excessive hemopoiesis in the liver, and hyperplasia of the islands of Langerhans are more frequently observed in infants with an excessive birth weight. It cannot be ascertained whether this is a true difference or not, since the data are too meager and the standards for evaluating anatomical changes in infants born before term are too uncertain. In comparing these data with those from other clinics it should be observed that the policy in the New York, New Haven, and Boston Lying-In Hospitals has been not to interrupt the pregnancies of diabetic women for other than obstetric reasons. Considerable differences may be found between the post-mortem material presented here and that from clinics where the policy is to terminate routinely the pregnancies of diabetic women a few weeks before term.

Roentgen examination of the hearts of newborn infants is generally regarded as of doubtful value. This feeling is based on the excellent studies of Weymuller, Bell, and Krahulik[21] and Dunham and D'Amico[22] and others who rightfully point out that there are considerable technical difficulties and that the results are quite variable and difficult to interpret. The present studies indicate that in spite of these handicaps,

roentgenography can be of great value in a study of groups of infants. The very significant difference between the normal and "diabetic" group of infants in the present study speaks for itself. In the case of a single infant serial examinations made at frequent intervals may be of diagnostic importance. Without the roentgen studies in this group of infants the diagnosis of cardiac enlargement would have been missed. The only peculiarity noted about the hearts on physical examination was that the heart sounds were louder than expected in a newborn infant. Cardiac murmurs were heard in some instances, but they were neither characteristic nor constant enough for diagnostic purposes.

SUMMARY

Cardiac enlargement has been demonstrated by roentgenography in ten infants born to mothers with diabetes mellitus. The cardiac enlargement which was marked during the first few days after birth became less, so that by the end of six weeks of life all evidence of enlargement had disappeared.

A large number of infants born to mothers with diabetes were found on post-mortem study to have cardiac hypertrophy, excessive amounts of erythropoiesis in the liver, and hyperplasia of the islands of Langerhans. These findings were observed more frequently in infants who weighed over 3,900 Gm. at birth than in those who weighed less than this amount. Macrosomia, cardiac hypertrophy, hemopoiesis in the liver, and hyperplasia of the islands of Langerhans were found associated together in three of the eighteen infants studied post mortem.

The same anatomical changes were observed in two stillborn infants born to mothers who subsequently became diabetic.

The possible association between the similarity of the anatomical picture in infants born to mothers with diabetes mellitus and in infants with erythroblastosis fetalis born to nondiabetic women is discussed.

CLINICAL CASES (TABLE I)

CASE 7.—N. H. H., No. B9835, female; hypoglycemia with cyanotic attacks and cardiac enlargement. The mother was a 26-year-old primipara who had had diabetes mellitus for one year. The Kahn test on her blood was negative. Pregnancy was uneventful except for a mild hydramnios. The diabetes was well regulated with about forty-five units of insulin daily. Labor occurred at term and she was delivered by low forceps with difficulty sixteen hours after the onset. The infant weighed 4,320 Gm. at birth and measured 53 cm. in length. She cried with stimulation and was given 95 per cent oxygen and 5 per cent carbon dioxide every fifteen minutes for the first few hours. Cyanosis of the face and extremities was present on the first day of life; petechiae were seen over the face; a systolic murmur was heard over the precordium, and there was a brachial palsy of the left arm. The blood sugars at the ages of 5 and 17 hours were 30 and 39 mg. per cent, respectively. On the second day it was noted that there were periods of cyanosis, that the cry was feeble and high pitched, and that the baby nursed poorly. The blood sugar concentration on the second day was 35 mg. per cent. By the fourth day the cyanosis had cleared and the baby seemed stronger, but the blood sugar was found to be 14 mg. per cent. The infant continued to do well during the

remaining six days in the hospital. On the eighth day the concentration of blood sugar was found to be 50 mg. per cent.

Roentgen examinations of the heart were made at 3, 8, and 11 days of age and at 3, 22, and 40 weeks of age. Marked cardiac enlargement was noted on the first examination. By the time the infant was 22 weeks of age the heart was normal in every respect on the roentgenograms. The systolic murmur, which had been heard at birth, was still present when the child was examined at 2 years of age. Persistent pupillary membranes were observed in both eyes. No other abnormalities were noted in the child.

CASE 8.—N. H. H., No. B11908, male; hypoglycemia with shock and marked cardiac enlargement. The mother was a primipara who was 19 years of age and had had diabetes mellitus for the past four years. Her diabetes was regulated by 80 units of insulin daily until the last part of pregnancy when the insulin was reduced to 35 units. Mild acidosis occurred at the third month. At the eighth month there was slight pitting edema of the legs, and her blood pressure rose to 140 systolic and 115 diastolic. The Kahn test on her blood was negative. Labor was induced two weeks before the expected date by artificially rupturing the membranes and lasted twenty-eight hours. Delivery was effected by low forceps without difficulty. The mother received 1/6 gr. of morphine before the delivery. The infant weighed 3,425 Gm. and measured 50 cm. in length. The baby did not breathe for two or three minutes and was given 95 per cent oxygen and 5 per cent carbon dioxide. Breathing was well established after four or five minutes. Examination of the infant at 12 hours of age revealed a baby with a weak cry and an ashen gray color to the skin. The heart sounds were louder than usual, and a gallop rhythm was present. A loud systolic murmur was heard. There was a palpable tumor mass in either flank extending to the crest of the ilium, which was taken to be kidney. The blood sugar was 16 mg. per cent. The infant received a hypodermocylsis of 100 c.c. of equal parts of normal saline and 5 per cent glucose and an infusion of 90 c.c. of 10 per cent glucose. On the second day there was some cyanosis of the hands and face. The nonprotein nitrogen of the blood serum was 45 mg. per cent. Total serum proteins were 5.6 Gm. per cent. There was albumin in the urine. The blood sugar concentration on the third day was 70 mg. per cent. The baby's course was satisfactory after the second day. The blood count was normal on four occasions. There were 2,250 erythroblasts per cubic millimeter on the second day of life and none thereafter.

The systolic murmur continued to be present until the end of the first month of life but has not been heard since on many examinations. Roentgenograms of the heart were made at 1, 2, 4, 8, and 15 days of age and at 2, 4½, 8, and 18 months of age. The heart and kidneys were notably enlarged on the first and second days. Some decrease in the size of the heart was noted on the fourth, eighth, and fifteenth days. The kidneys also were smaller by the fifteenth day, and an intravenous pyelogram at that time was normal. The roentgenograms showed the heart was still large at 2 months of age and questionably enlarged at 4½ and 8 months of age. The last examination at 18 months of age was entirely negative. He was last examined at 20 months of age in the cardiac clinic, where no evidence of heart disease was found.

CASE 9.—N. H. H., No. B32972, female; hypoglycemia with marked cyanosis and cardiac enlargement. The mother was 35 years of age and had had diabetes mellitus for the past seven years. This was her second pregnancy. The first child was born five years previously and has been reported (Case 2[1]). Her diabetes was well regulated throughout the second pregnancy by the daily administration of about 90 units of insulin. During the last trimester there was a mild albuminuria and slight pitting edema of the legs. The Kahn test on the mother's blood was nega-

tive. One month before the expected date the infant was born by cesarean section. The infant weighed 3,280 Gm. and was 47.5 cm. in length. She cried spontaneously and had a good color at birth. Within four hours marked cyanosis appeared all over. The baby cried in a moaning fashion. She was sluggish and sleepy. The respirations were ninety per minute. The heart sounds were strong. The baby was placed immediately in an oxygen tent and the cyanosis cleared. At 8 hours of age the blood sugar concentration was 14 mg. per cent. She received 65 c.c. of a 5 per cent solution of glucose beneath the skin. The infant could not be removed from the oxygen tent until the sixth day without becoming cyanotic. Blood sugar concentrations at 2, 4, 6, 8, and 10 days of age were 45, 23, 40, 23, and 66 mg. per cent, respectively. The baby was removed permanently from the oxygen tent on the seventh day and continued to progress satisfactorily until discharge on the sixteenth day. The blood count on the first day was normal. No mention of erythroblasts on the blood smear was made. Roentgen examinations were done on the first and tenth days. A markedly enlarged heart was observed on the first day, and a considerable diminution in size was noted by the tenth day. No further follow-up examinations have been made.

CASE 10.—N. H. H., No. B33765, female; hypoglycemia with cyanosis and dyspnea and cardiac enlargement. The mother was 37 years of age. She had had diabetes mellitus for thirteen years. This was her second pregnancy, the first having resulted in a stillbirth as the result of a difficult delivery of a large fetus that weighed 9 pounds 1 ounce, two years previously. The diabetes was well controlled throughout the second pregnancy by the daily administration of about 40 units of insulin. During the eighth month pitting edema of the legs appeared, the blood pressure rose to 155 systolic and 95 diastolic, and albumin was present in the urine. Hydramnios was marked. The Kahn test on the mother's blood was negative. The infant was born one month before the expected date by cesarean section. She weighed 3,720 Gm. at birth and was 50 cm. in length. Respirations were not established until five minutes after birth. The baby remained cyanotic. Artificial respiration was given in conjunction with 95 per cent oxygen and 5 per cent carbon dioxide. After about fifteen minutes the child was breathing regularly and voluntarily. She remained cyanotic, particularly about the hands and feet. Pitting edema was present over the dorsum of the feet and legs. The heart was normal by physical examination. The baby was placed in an oxygen tent where she remained for the next twelve days. The cord blood sugar concentration was 28 mg. per cent, and four hours later the baby's blood sugar was 15 mg. per cent. Total serum proteins of the cord blood were 6.5 Gm. per cent; and of the baby's blood serum four hours later, 5.9 Gm. per cent. She received 65 c.c. of a 5 per cent solution of glucose by hypodermoclysis at 7 hours of age. On the second day her respirations in the oxygen tent were periodic and were counted at 135 per minute, although cyanosis was not present. Drowsiness was notable. By the third day the respirations were 90 per minute. The infant became cyanotic when taken out of the tent. Transient twitching of the hands was noted. On the fourth day the respirations were no longer labored or rapid. The edema of the feet which had been present up to then disappeared. She was much improved but had to be kept in the oxygen tent for the next eight days since she became cyanotic when removed. The infant was discharged on the seventeenth day, her physical examination being negative. A blood count done on the first day was normal. Erythroblasts were 1,700 per cubic millimeter on the first day. Roentgenograms were made of the heart at 1, 4, and 11 days of age and at 6 weeks of age. Marked cardiac enlargement was observed on the first day with a reduction of cardiac size on each subsequent examination. However, the heart had not yet returned to normal by the time of the last roentgenogram at 6 weeks of age, although by physical examination the heart and baby both were entirely normal.

AUTOPSIED CASES (TABLE III)

CASE 7.—N. H. H., No. 33528, male, born in 1929. The mother was 34 years of age and had had diabetes mellitus for the previous five years. The Wassermann test on the mother's blood was negative. This was her seventh pregnancy. Three previous pregnancies had ended in stillbirths, two in miscarriages and one in a living child. The present pregnancy was uneventful except for some edema of the legs in the last months. The diabetes was well regulated on from 10 to 15 units daily. Delivery was effected by cleidotomy because of severe dystocia. The fetal heart sounds were heard prior to delivery. The birth weight was 5,070 Gm.

CASE 8.—N. H. H., No. 68195, male, born in 1928. The mother was 42 years of age. This was her ninth pregnancy. Seven previous pregnancies resulted in living children and one in a miscarriage. The present pregnancy was uneventful. A fasting blood sugar was 75 mg. per cent on the day before delivery. After a difficult labor the fetus was born dead. It weighed 5,490 Gm. Two examinations of the mother's urine during the postpartum period were negative for reducing substances when tested with Benedict's solution. The mother came to the metabolism clinic five and a half years later. Polydipsia, pruritis of the vulva, and nocturia had been present for the past four years and she had lost thirteen pounds in the previous twelve months. Her urine on this admission showed complete reduction with Benedict's solution. A diagnosis of diabetes mellitus was made. During the next six months she was on a low carbohydrate diet and under this regime her urine gradually became free of sugar. Her subsequent history is unknown. The Kahn test on her blood was negative.

CASE 9.—N. H. H., No. 68034, male, born in 1939. The mother was 21 years of age. This was her third pregnancy. One previous pregnancy resulted in a miscarriage and the second one in a living child. The present pregnancy was uneventful except for polyhydramnios and a mild toxemia. Labor was difficult, and the infant was stillborn. The birth weight was 5,850 Gm. A fasting blood sugar done at the time of delivery was 68 mg. per cent. Two urine examinations done during the postpartum period were negative for reducing substances. The mother, however, failed to recover her previous good health, was fatigued, and failed to gain weight. Four months after the delivery polydipsia and frequency appeared. She was admitted to the hospital five months after her confinement because of these symptoms and a loss of twenty pounds in the previous two weeks. Fasting blood sugars ranged from 200 to 400 mg. per cent. She was followed in the metabolism clinic for the next seven months, during which time her diabetes was well regulated on from 60 to 100 units of insulin a day in divided doses. The Kahn test on the mother's blood was negative.

CASE 16.—N. H. H., No. A50281, male, born in 1935. The mother was 25 years of age and had had diabetes for ten years. This was her fifth pregnancy. Two previous pregnancies ended in miscarriages, one in stillbirth, and one in a living child. The present pregnancy was uneventful. Delivery occurred spontaneously at the eighth month. The child weighed 6 pounds. On the second day of life he was noted to be sleepy and there were some twitchings of the toes. He was admitted to the hospital on the third day of life. Blood cultures and cultures of the cerebrospinal fluid showed hemolytic staphylococci. Death occurred on the thirteenth day. The Kahn test on the baby's blood was negative.

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STUDIES OF NITROGEN AND FAT METABOLISM ON INFANTS AND CHILDREN WITH PANCREATIC FIBROSIS

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DURING the past few years pancreatic fibrosis has been observed and recognized with increasing frequency in pediatric clinics. Important features of the disease have been summarized by Andersen,[1] Blackfan and May,[2] and Jeffrey.[3] The studies of pancreatic enzyme activity by Anderson and Farber and Maddock[4] have furnished a diagnostic method of practical importance. The pathologic and experimental studies reported by Farber[4a] indicate that this disease is one involving many parts of the body even though the pancreatic lesion may dominate the picture. A large number of infants and children with pancreatic fibrosis has been observed at the Infants' Hospital and the Children's Hospital.*

So far as we are aware, no metabolic studies on pancreatic fibrosis in children are available. For such information we have only the analogy to observations on experimental animals. By far the most interesting and important of these are the studies of Pratt and associates, continued over a period of thirty-five years. In 1909, with Lamson and Marks,[5] he demonstrated the function of the external secretion of the pancreas. When the pancreatic ducts were tied off, dogs survived for long periods of time. They produced large bulky stools, up to one-fourth of the total body weight. The weight of the dried feces was as much as ten times that of unoperated animals, and the nitrogen and fat were increased. These findings have not been extended significantly, in spite of all the intervening work which has been summarized by Ivy[6] and by Pratt.[7]

Pancreatic fibrosis in children has not been commonly recognized at an early stage in the disease. It was hoped that a study of metabolism would add to an understanding of pathologic physiology, perhaps assist the clinician to establish the diagnosis relatively early, to differentiate it from other conditions of less grave prognosis, and to serve as a guide to rational therapy.

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*Various aspects of the condition of pancreatic fibrosis have been studied in these hospitals and the investigations are about to be published. These include roentgenologic studies by Dr. E. B. D. Neuhauser, studies of pancreatic enzyme activity in the celiac syndrome, and the effect of secretin on the flow of pancreatic juice in early life by Dr. S. Farber, Dr. C. L. Maddock, and Dr. H. Shwachman, and the pathologic characterization of the disease and experimental studies on the production of the experimental lesion by Dr. S. Farber. The autopsy numbers and the hospital numbers are given to permit cross identification of the patients in all of these studies.

When pancreatic juice of dogs is excluded from the intestine, the digestion of protein is most markedly affected, fat next, and carbohydrate least.[6] For this reason we decided to study the nitrogen metabolism and fat excretion of infants with pancreatic fibrosis.

EXPERIMENTAL

The plan was to make observations of nitrogen balance and of fat excretion on children with pancreatic fibrosis. To determine metabolism under usual conditions the children were fed a normal diet; that is, milk formula for infants and the Hospital House Diet for children. For the purposes of this discussion we have grouped these together as intake type I. Similar observations were made to study the alteration in metabolism when no native protein was given; for this the infants were fed a prepared food containing hydrolyzed casein, fat, and starch, but no native protein* (type II). Observations also included periods when casein hydrolysate† and glucose, a mixture containing neither protein, polysaccharide, nor fat (type III), was given intravenously, subcutaneously, or orally. In addition, pancreatin‡ was administered during some periods when a mixed diet was fed (type IV) in an effort to determine whether the restoration of the missing enzymes would correct the defective metabolism. We used enteric-coated granules of prancreatin to prevent gastric digestion. We have found that the pancreatic juice recovered from patients with pancreatic fibrosis was sufficiently alkaline to dissolve the covering on these granules and allow them to exert their enzymic activity. The preparation we used has been tested in our laboratory for enzyme content and found to be relatively high in trypsin and low in lipase. One gram was equivalent to the trypsin in 40 c.c. of the duodenal juice of normal infants, but to the lipase, less than 0.2 c.c. of juice.

The patients were placed upon metabolism beds.§ Collection periods were of three to five days' duration. Carmine was given as a marker. The urine and feces were analyzed separately when possible. The feces were dried to constant weight on a steam bath. The nitrogen content of the food, urine, and feces was determined by the Kjeldahl method, and the fat content of the feces, by the method of Tidwell and Holt.[5] Of the stools tested, none were found to contain starch or sugar. As is usual in this disease, glucose tolerance tests gave low values. No further studies on the carbohydrate metabolism in this disease were made.

*This was a mixture of 20 per cent casein hydrolysate (Amigen), 42.3 per cent dextrimaltose, 10 per cent starch, 18 per cent olive oil, 3 per cent brewers' yeast, and 6.7 per cent salts. This product was prepared by and supplied through the courtesy of Mead Johnson & Co. A Mead Johnson product is now available under the trade name of Nutramigen which is identical with the preparation we used except that it contains corn oil instead of olive oil.

†This material, Amigen, was prepared and supplied through the courtesy of Mead Johnson & Co. Amigen contains no unhydrolyzed protein. The nitrogen is present in various forms; about 60 per cent is amino nitrogen.

‡Parke, Davis & Co. enteric granules, triple strength, 5 gr., salol coated. Dosage, 4 to 8 capsules.

§The patients were under the nursing care of Miss Harriet O'Hara, to whom we are indebted for careful collection of material.

We present data on nine patients with pancreatic fibrosis, of whom only three are still living, and one of these is not expected to live long. The diagnosis was established by enzyme analyses of the duodenal fluid, and in those patients that later succumbed, by pathologic examination. Both hospital and autopsy numbers of the patients are given so that the metabolic data on each case may be studied in conjunction with the other aspects as published separately.

We have also data on six infants who served as "sick controls." They were severely ill or suffering from chronic diseases as follows: One child (M. F.) with celiac syndrome has subsequently improved markedly; two infants (D. C. and P. C.) had severe eczema; one (R. W.), fatal septicemia; and two (G. P. and C. T.), chronic nutritional disturbance. These infants were not gaining weight, but had no symptoms that might be referred primarily to the pancreas. For further comparison we present data taken from our previous studies[9] and from the literature on normal infants and children on similar regimes.

RESULTS

The data are presented in Table I. The intakes are classified under four categories, as explained under the plan of the study. The periods of observation are listed chronologically for each infant. The order in which the different types of intake were given was varied intentionally so as to avoid effects in one period which might be traceable to the previous period. Observations on all four types of intake were obtained in only one patient (M. H.) In order to facilitate comparison of results according to the type of intake, summaries of the data in Table I have been made in Tables II to V.

The data are expressed both as grams per day and as grams per kilogram per day for this reason: the totals per day alone do not allow for the fact that larger children eat more and have more feces; on the other hand, the output of feces is not proportional to body weight, so that the expression as grams per kilogram also gives a distorted impression. Expression as grams per day gives undue importance to data on older children, and grams per kilogram per day, to the data on younger children. Even the fat, which Macy[10] has shown to be proportional to body weight in older children, cannot be fairly expressed as grams per kilogram for infants. A true standard for comparison probably lies somewhere between the two methods. Only one case of an older child is included in our data (W. H.), and this does not throw the averages out of line, for, although he was 11 years old, his weight was that of a normal 4 year old.

Individual cases showed wide variation due to age and size of the patient, the stage of the disease, and other factors which are unknown or were beyond control. Each value in Tables II to V is an average of the results of from 3 to 10 periods. The observations are too few and the variables too many for further statistical analysis.

TAB

NAME	AGE	HOSPITAL NO.	DATE OF DEATH	AUTOPSY NO.	WEIGHT (KG.)	DATE	IN TYPE*	IN METHOD OF ADMINISTRATION
								Patients With
W. H.	11 yr.	183,968			18.7	8/ 8 to 8/11/41	I	Oral
					18.0†	8/13 to 8/17/41	IV	Oral
					18.7	9/ 6 to 9/10/41	II + IV	Oral
R. D'A.	5 mo.	240,310	4/ 3/40	A-40-58	5.1	3/26 to 3/29/40	I	Oral
						3/29 to 3/31/40	III	Intravenous
S. M.	8 mo.	242,814	8/14/40	A-40-127	4.5	7/29 to 8/ 1/40		
					4.2	8/ 2 to 8/ 5/40	II	Oral
							III	Intravenous
					4.0‡	8/ 5 to 8/10/40	III+ Blood	Intravenous
B. P.	14 mo.	243,092	8/17/40	A-40-128	5.5	8/ 5 to 8/ 9/40	I	Oral
					5.4	8/ 9 to 8/13/40	II	Oral
					5.0	8/14 to 8/17/40	III	Intravenous
G. L.	5 mo.	243,659	9/18/40	A-40-139	4.6	8/17 to 8/20/40	I	Oral
					4.9	8/25 to 8/28/40	III+ Blood	Intravenous
					4.2	9/14 to 9/17/40	II	Oral
R. McG.	16 mo.	248,898	2/17/41	A-41-28	7.6	2/12 to 2/14/41	I	Oral
J. S.	9 mo.	251,775			4.6	8/28 to 9/ 2/41	II	Oral
					4.7	9/ 6 to 9/11/41	I	Oral
					4.9	9/12 to 9/17/41	III	Oral
B. H.	19 mo.	254,341			7.5	8/21 to 8/26/41	II	Oral
					7.7	9/ 2 to 9/ 7/41	I	Oral
M. E. H.	4 yr.	254,906	12/10/42	A-42-178	12.3	6/ 5 to 6/ 8/42	I	Oral
					12.5	6/11 to 6/14/42	II	Oral
					12.1	6/18 to 6/21/42	IV	Oral
					11.5	6/25 to 6/28/42	I	Oral
							III	Subcutaneous
					11.7	7/ 1 to 7/ 4/42	I	Oral
			DISEASE					*Sick*
M. F.	14 mo.	239,680	Celiac		7.2	2/29 to 3/ 2/40	I	Oral
					6.8	3/ 2 to 3/ 9/40	III + Blood	Intravenous
D. C.	5 mo.	242,521	Eczema		4.6	7/24 to 7/27/40	I	Oral
R. W.	7 mo.	243,363	Eczema, septicemia Died 9/13/40		5.3	8/18 to 8/21/40	III + Blood	Intravenous
					6.8	8/21 to 8/24/40	I + Blood	Oral / Intravenous
					6.8	8/25 to 8/28/40	II	Oral
P. C.	19 mo.	230,464	Eczema		8.9	9/ 6 to 9/ 9/40	I	Oral
					8.9	9/21 to 9/25/40	II	Oral
C. T.	9 wk.	245,958	Chronic nutritional disturbances		4.6	10/ 7 to 10/11/40	I	Oral
G. P.	10 mo.	247,855	Chronic nutritional disturbances		4.5	2/ 6 to 2/ 9/41	I	Oral
					4.4	2/11 to 2/13/41	III	Oral
					4.4	2/13 to 2/16/41	III	Oral
					4.8	2/24 to 2/27/41	II	Oral

*Type I: Milk formula for infants and Hospital House Diet for children.
Type II: Nutramigen (see * on page 268).
Type III: Amigen (see † on page 268) plus glucose solution.
Type IV: Type I plus pancreatin (see ‡ on page 268).

LE I.

INTAKE			OUTPUT							NITROGEN BALANCE	
	NITROGEN				FECES						
CAL. PER KG. PER DAY	GM. PER DAY	GM. PER KG. PER DAY	TOTAL NITROGEN (GM. PER DAY)	URINE NITROGEN (GM. PER DAY)	DRY WEIGHT (GM. PER DAY)	NITROGEN (GM. PER DAY)	NITROGEN (PER CENT OF INTAKE)	NITROGEN (PER CENT OF OUTPUT)	FAT (GM. PER DAY)	GM. PER DAY	GM. PER KG. PER DAY
Pancreatic Fibrosis											
80	8.00	0.43	8.36	3.96	81.2	4.40	55	53	26.5	−0.36	−0.02
80	8.00	0.44	4.52	2.90	30.9	1.62	20	36	10.9	3.48	0.19
90	9.30	0.50	7.91	6.24	45.6	1.67	18	21	13.9	1.40	0.08
100	2.58	0.51	1.40	0.82	10.9	0.58	22	43		1.18	0.22
65	2.52	0.50	2.17	1.80	5.8	0.37	14	20		0.35	0.07
65	1.76 0.73	0.60	2.25							0.24	0.06
80	2.00 0.32	0.58	2.54							−0.22	−0.05
45	1.56	0.28	1.77							−0.21	−0.04
50	1.12	0.21	1.74							−0.62	−0.11
	4.13	0.82	2.21							1.92	0.38
90	1.78	0.61	1.34	0.61	13.8	0.73	41	55	5.9	0.44	0.10
60	3.07 0.83	0.80	1.57	1.36	2.1	0.21	5	14	0.2	2.33	0.48
120	2.48	0.59	1.91	0.92	27.3	0.99	40	52	14.6	0.57	0.13
80	4.50	0.59	3.61	2.49	29.6	1.12	25	31		0.89	0.12
140	3.08	0.68	2.78	2.14		0.64	20	23		0.30	0.06
165	5.52	1.18	4.39	2.18		2.21	40	50		1.13	0.24
105	5.30	1.08	3.52	2.94		0.58	11	16		1.78	0.37
120	4.14	0.52	4.71	3.73		0.98	24	21		−0.57	−0.08
130	7.30	0.91	6.25	4.50		1.75	24	28		1.05	0.14
60	4.98	0.41	3.75	2.61	27.6	1.14	23	30	12.7	1.23	0.10
50	5.05	0.40	4.73	3.49	36.2	1.24	24	26	19.5	0.32	0.03
60	5.34	0.44	4.94	4.21	31.0	0.73	14	15	21.0	0.40	0.03
	2.43 1.46	0.34	3.40	2.33	22.3	1.07	28	32	8.0	0.49	0.04
	5.32	0.46	6.03	3.81	48.3	2.22	41	36	22.3	−0.71	−0.06
Controls											
	0.66	0.10	1.40	1.40						−0.74	−0.10
90	3.43 0.87	0.60	2.90	2.65	2.7	0.25	6	9		1.40	0.21
100	2.50	0.54	1.46	1.30	4.7	0.16	6	11	1.7	1.04	0.21
60	2.93 0.87	0.50	2.56	2.39	2.4	0.17	5	7	0.2	1.24	0.24
70	3.60 1.05	0.68	2.14	1.61	10.5	0.53	11	25	1.9	2.51	0.37
70	2.25	0.33	1.71	1.10	11.4	0.61	28	36	1.8	0.57	0.08
70	4.85	0.54	3.88	3.25	15.0	0.63	12	16	5.3	0.98	0.11
85	2.88	0.32	2.76	2.48	7.7	0.28	10	10		0.10	0.01
100	2.25	0.49	1.51	1.31	3.5	0.20	9	18	1.0	0.74	0.16
110	3.90	0.87	2.98	2.65	11.6	0.33	8	11	5.3	0.92	0.20
220	7.25	1.65	5.37	5.28	4.1	0.09	1	2	2.1	1.88	0.43
220	7.26	1.65	4.90	4.78	2.9	0.12	2	3	1.1	2.36	0.53
125	2.80	0.59	2.58	2.22	11.9	0.36	13	14		0.22	0.44

†Gained 450 Gm. by 8/20/41.
‡Gained 500 Gm.

Weight of the Feces.—The data on the weight of the feces are given in Table II. It is clear that patients with pancreatic fibrosis have more feces than those with other diseases or normal infants and children. When native protein was removed from the diet (type II), the weight of the feces was as great as when it was included, but when both protein and fat were omitted and the nutriment given parenterally (type III), the residue of the feces was small, and, although not so small as for normal infants on similar diet, it was below that of normal infants on usual diets. Pancreatin in the amounts given (type IV) reduced the weight of the feces but not to the normal level.

TABLE II

AVERAGE WEIGHTS OF DRIED FECES PER DAY

CASES	TYPE OF INTAKE							
	I		II		III		IV	
	GM.	GM. PER KG. OF BODY WEIGHT	GM.	GM. PER KG. OF BODY WEIGHT	GM.	GM. PER KG. OF BODY WEIGHT	GM.	GM. PER KG. OF BODY WEIGHT
Pancreatic fibrosis	33.4	3.2	31.7	4.5	2.8	0.7	35.8	2.3
Sick controls	9.1	1.5	10.3	1.7	3.0	0.6		
Normal infants[1]	7.3	1.2	4.4	0.7	1.5	0.4		
Normals, 4 yr.[2]	15.0	0.8						

[1]Reference 9.
[2]Reference 10.

The data show that qualitative differences in the diet were significant factors in the amount of feces produced. But quantitative differences were also significant. If the food is increased beyond the capacity to digest and absorb it, the amount of feces is greater. For example, a patient with pancreatic fibrosis,[11] fed a milk modification at a level of 50 calories per kilogram per day, produced only 6.5 Gm. (dry weight) of feces per day. When the same food was given at a level of 100 calories, she produced 55 Gm. This is an exact counterpart of the data for dogs reported by Pratt. We are at present trying modifications of a test diet which we hope will give even more strikingly clear-cut differentiation between normal infants and those with pancreatic fibrosis.

Nitrogen Metabolism.—The values for the excretion of nitrogen in the feces are given in Table III. The amounts of nitrogen in the feces of patients with pancreatic fibrosis are large; in fact, they may *exceed the amounts found in the urine.* The average fecal nitrogen, in proportion to the total nitrogen excretion, is three or four times that of normal infants.

The amount of nitrogen per unit of weight of the feces shows very little variation between normal infants and those with pancreatic fibrosis. The total amount of nitrogen in the feces of the patients with pancreatic fibrosis was greater than that in other groups, principally

TABLE III

AVERAGE NITROGEN CONTENT OF THE FECES PER DAY

CASES	TYPE OF INTAKE											
	I			II			III			IV		
	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF OUTPUT	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF OUTPUT	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF OUTPUT	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF OUTPUT
Pancreatic fibrosis	1.70	0.20	40	0.96	0.13	30	0.39	0.08	17	1.3	0.08	24
Sick controls	0.35	0.06	15	0.41	0.06	20	0.16	0.03	5			
Normal infants[1]	0.39	0.07	14	0.32	0.05	11	0.05	0.01	3			
Normals, 4 yr.[2]	1.07	0.06	12									

[1]Reference 9.
[2]Reference 10.

TABLE IV

AVERAGE NITROGEN INTAKES AND BALANCES PER DAY

CASES	TYPE OF INTAKE											
	I			II			III			IV		
	INTAKE	BALANCE		INTAKE	BALANCE		INTAKE	BALANCE		INTAKE	BALANCE	
	GM. PER KG. OF BODY WEIGHT	GM. PER KG. OF BODY WEIGHT	PER CENT OF INTAKE	GM. PER KG. OF BODY WEIGHT	GM. PER KG. OF BODY WEIGHT	PER CENT OF INTAKE	GM. PER KG. OF BODY WEIGHT	GM. PER KG. OF BODY WEIGHT	PER CENT OF INTAKE	GM. PER KG. OF BODY WEIGHT	GM. PER KG. OF BODY WEIGHT	PER CENT OF INTAKE
Pancreatic fibrosis	0.57	0.09	16	0.38	-0.05		0.75	0.25	33	0.46	0.10	22
Sick controls	0.54	0.16	30	0.59	0.04	7	0.95	0.35	37			
Normal infants[1]	0.70	0.17	24	0.62	0.14	23	0.73	0.20	27			
Normals, 4 yr.[2]	0.52	0.04	7									

[1]Reference 9.
[2]Reference 10.

because the weight of the feces was greater. Therefore we have given the total amounts of nitrogen and the amounts per kilogram of body weight rather than the concentration of nitrogen in the feces.

The patients with pancreatic fibrosis excreted a great deal more nitrogen in the feces than did the sick controls or the normal infants and children, with each of diets type I, II, and III. But with type III, the average amounts of fecal nitrogen of patients with pancreatic fibrosis was as low as that of normal infants and children fed usual diets. With pancreatin added to the diet (type IV), the values for nitrogen in the feces of the patients with pancreatic fibrosis (similarly to those for weight of the feces) were midway between the high values found when these patients were fed type I diets and the low values of normal infants fed type I diets.

The data for nitrogen balances have been summarized in Table IV. They show that positive nitrogen balances can be obtained in infants and children with pancreatic fibrosis with several types of diet. This group retained less nitrogen per given intake than any other group when fed House Diet or milk modification (type I) or the food which contained fat but no native protein (type II). On type II diet they showed both positive and negative balances; the average was a negative balance of small degree at an average level of intake which would uniformly result in positive balances in normal individuals.[15] That this was not due to the type of diet is shown by the fact that individuals did have positive balances on this diet when the intake was comparable to the intake on the type I diet. For example, G. L. (September 14 to 17) had a positive balance of 0.13 Gm. per kilogram with an intake of 0.59, which is an even better retention than the average of his group when fed type I diet.

When the nutriment was given parenterally (type III), the retentions of the patients with pancreatic fibrosis were considerable. They were as great as those of normal infants on similar regimes. The nitrogen intakes were larger than these sick infants would take by mouth. Higher percentages of the intake were retained than with type I or type II feeding; this was due in part to increased intake, and in part to increased efficiency in utilization. The increase in retention (from 16 to 33 per cent of the intake) was greater for the patients with pancreatic fibrosis than for the sick controls (from 30 to 37 per cent).

Long experience has shown that the amount of nitrogen retained is dependent upon the level of intake. When the nitrogen intake is too low, the balance is negative; when adequate, a normal infant will retain roughly from 20 to 30 per cent of the intake. With generous intakes both the amount and the percentage of the intake retained are considerably greater. With excessive intakes retentions may become smaller both relatively and absolutely.[12] These facts are illustrated in Table IV. That nitrogen retentions were larger when the intakes were greater is shown by comparing the balances of patients in one group

TABLE V

AVERAGE FAT CONTENT OF DRIED FECES PER DAY

CASES	TYPE OF INTAKE											
	I			II			III			IV		
	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF DRIED FECES	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF DRIED FECES	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF DRIED FECES	GM.	GM. PER KG. OF BODY WEIGHT	PER CENT OF DRIED FECES
Pancreatic fibrosis	16.8	1.2	41	17.0	2.2	54	0.2	0.04	5	14.9	1.0	42
Sick controls	3.0	0.4	30	2.9	0.2	21	0.6	0.12				
Normal infants	3.1[1]	0.5	35	1.7[2]	0.3	29						
Normals, 4 yr.[3]	1.6	0.1	11									

[1]Reference 13.
[2]Reference 11.
[3]Reference 10.

on all diets (reading across) or by comparing the patients in different groups on the same diet (reading down). Although the nitrogen retentions of the patients with pancreatic fibrosis increased when the nitrogen intake increased, this result was accomplished with poor economy; a smaller percentage of the intake was retained and more was excreted in the feces. This inability to profit by larger intakes occurred at a level of intake which is well within the range of optimal intakes for normal children.

Fat Metabolism.—The average values for fat in the feces are given in Table V. When fed either type I or type II diet the patients with pancreatic fibrosis had much more fat in the feces than the other groups of cases, both absolutely and in grams per kilogram of body weight and also in percentage of the dry feces. The amount of fat lost by patients with pancreatic fibrosis when fed type I diet averaged 1.2 Gm. per kilogram of body weight. This amounts to about 11 calories per kilogram, which represents a serious loss in energy value, about one-third of the fat or one-fifth of the total caloric intake. This is more than five times the normal loss, which is about 10 per cent of the fat intake in infants[13] and 5 per cent in children.[10] We were not able to demonstrate any significant difference in the fat in the feces when pancreatin was added to the diet (type IV). These patients who showed poor utilization of the fat also had poor vitamin A absorption curves.[14]

When given a fat-free diet parenterally (type III), the fat in the feces was diminished for both the patients with pancreatic fibrosis and the sick and normal controls, but even more for the former than the latter. We do not wish to emphasize the difference between the patients with pancreatic fibrosis and the sick controls on the point of fat excretion as some of the controls may have had difficulty with fat metabolism. The main deduction from these data is that a fat-free parenteral diet is well utilized by patients with pancreatic fibrosis. Only two patients in this series were given the type III diet orally (J. S., pancreatic fibrosis; and G. P., chronic nutritional disturbance). Each showed excellent nitrogen retention. Moreover, in other studies on infants with acute gastrointestinal disturbances, we have shown that there was no difference in nitrogen retention whether casein hydrolysate was given orally or parenterally.[15] Therefore it seems probable, although it has not been proved, that the good nitrogen retentions were due to the absence of fat rather than to the method of administration.

The presence of fat in the feces when no fat was given raises the further interesting question of the nature of fat in these cases and the endogenous production of fat. It is important to have more data on this subject, especially on results with diets containing protein and minimal amounts of fat, and with the casein hydrolysate and glucose given orally.

DISCUSSION

The data presented show a marked similarity to those found in experimental animals when the pancreatic ducts were tied off and the

external secretion of the pancreas prevented from entering the intestine—increase in bulk of the feces and wastage of nitrogen and fat.

Fecal nitrogen and fat are frequently spoken of as unabsorbed; we have referred to them as excreted. Even if the material is unabsorbed, it is undoubtedly altered during the course of its passage through the intestinal tract. When no nitrogen was given orally and no fat was given at all, both nitrogen and fat were found in the feces. Whether these were present in the bodies or products of bacteria or whether they were true secretions or excretions is not known. Certainly they were not unabsorbed. Until stronger evidence accumulates as to the exact form of the fecal nitrogen and its source, we consider it better to allude to this material as excreted.

In pancreatic fibrosis, the striking feature of nitrogen metabolism is the excessive nitrogen found in the feces rather than the poor nitrogen balances, although these patients make poorer gains than normal infants and often have negative nitrogen balances. On the whole, on moderate intakes they show fair retentions, although below that of normals. Excessive nitrogen in the feces is the cause of the negative nitrogen balance and is partly responsible for the loss of weight and clinical deterioration so prominent late in this disease. Excessive nitrogen in the feces is a concomitant of excessive weight of the feces. High fat content of the feces is a characteristic of this disease, but there are other conditions which affect the fat metabolism even more markedly than does pancreatic fibrosis. The difference between the weight of the feces of patients with pancreatic fibrosis and that of other sick children and normals is so great, and the evidence is so easy to obtain that it should be available to every physician as a distinct aid in diagnosis, as has been strongly emphasized by Pratt.

In our experience, administration of pancreatin did not lead to any improvement in fat metabolism. However, we have made too few observations with pancreatin to pass judgment on its value. It is well known that fat metabolism varies greatly from case to case under the same conditions. Various preparations of pancreatin differ in their enzyme content both qualitatively and quantitatively. Available preparations are low in lipase and therefore could not be expected to aid in the utilization of fat (see* on page 270).

Because of the fatal outcome of pancreatic fibrosis, any rational type of therapy would be welcome. There are two methods of approach. The progress of the disease might be arrested by giving a diet which is not beyond the digestive capacity of the patient. This is similar to giving a low carbohydrate diet to diabetic patients. Because even very moderate amounts of protein are not dgested and absorbed, and generous amounts of casein hydrolysate are utilized, hydrolyzed casein plus carbohydrate seem to offer improved dietetic therapy. A second method is substitution therapy. To continue the analogy, the use of pancreatin in pancreatic fibrosis is similar to the use of insulin in dia-

betes in that the former makes good an enzyme deficit and the latter makes good a hormone deficit. Even though, in our experience, pancreatin did not benefit nitrogen metabolism as much as parenteral administration of hydrolyzed casein and glucose, the two types of therapy might well be used together. The oral administration of this type of diet is now being studied.

The data presented cannot be expected to show therapeutic success. They are presented in the hope that others may try these diets or modifications of them over long periods of time.

SUMMARY

Infants and children with pancreatic fibrosis have shown a type of metabolism which closely approximates that described in dogs with blocked pancreatic ducts. It is characterized by feces with a high residue and large nitrogen content; the fat is moderately increased. When fed a diet containing nitrogen but no native protein, the dry weight, nitrogen content, and fat of the feces were little affected. Addition of pancreatin to a diet containing both protein and fat was followed by some reduction in the amount and nitrogen content of the feces but caused no change in fat excretion. The amount of fecal excretion and the nitrogen in the feces were reduced to within normal limits when a fat-free ration consisting of casein hydrolysate and glucose was administered.

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SKIN DISEASE OF THE NEWBORN INFANT

Consideration of the Relationships Between Leiner's and Ritter's Disease, With Case Report

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THE skin affections of the newborn infant are still a major problem in the modern hospital nursery. Scrupulous precautions are taken to eliminate any possible source of infection. Laudable and necessary as this has been, it has, unfortunately, resulted in neglecting further research to determine the underlying cause. Most of us accept only too readily bacterial infection as the primary cause, although the literature reveals that deeper organic causes have been considered. An extensive study of a case, which we have hesitatingly called Leiner's disease (though I do not believe this disease to be an entity), has stimulated our interest in this important pediatric problem. As a result of this study—later correlated with a review of the literature—the conclusion has been suggested that the underlying cause is a temporary dysfunction of the endocrine system. The dysfunction in the majority of infants probably originates in the mother, who has to adapt herself physiologically to demands put on her endocrine system during pregnancy.

In the more severe cases of skin diseases, such as pemphigus neonatorum, which has been accepted as identical with Ritter's disease,[14, 63] more is known of the histopathology because of the higher mortality. Of Leiner's disease less is known[30] because it is less often fatal and also is less prevalent in this country.

Pemphigus neonatorum and Ritter's disease first manifest themselves by a local hyperemia of the skin. Bullae may develop, appearing in crops and spreading all over the body. The skin becomes wrinkled and exfoliation occurs. This is sometimes so marked that large portions of the epidermis can be detached. Nikolsky's sign is positive. In Leiner's disease the skin is inflamed but not ulcerated, and seborrhea of the scalp is characteristic. The trunk is red; the scales are grayish white, opaque at first but later somewhat lustrous. Nikolsky's sign* is absent. Furthermore, vomiting or some diarrhea is present in almost every case at this stage. The face and extremities may become cyanotic. Later the extremities become hypertonic and the skin looks dry like parchment. Finally, diarrhea and cachexia may occur in the terminal stage.

Clinically, it is often difficult to distinguish between Ritter's and Leiner's diseases.[30, 33] Some authors write of desquamation and exfoliation as synonymous in the same paragraph. Even if everyone

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*When slight pressure or friction is exerted on what appears to be normal skin, the upper layers of the epidermis become separated. This is caused by a diminution of the adhesion between the stratum corneum and the subjacent layers.

agrees that Nikolsky's sign is present in Ritter's and absent in Leiner's disease, there are marked discrepancies as to the histopathology of the skin. A case with positive Nikolsky's sign may show definite inflammatory cell infiltration of the skin,[9] although these inflammatory cells are presumably not characteristic of Ritter's disease.[3] In Leiner's disease, on the other hand, where the cellular infiltration should be abundant, it may be so scant as to be almost negligible.

Another characteristic feature of Ritter's disease is said to be separation of the stratum granulosum of the epidermis. This has been reported by Kendall and Aegerter,[31] Guy and Cohen,[22] and others.[9] Atrophy of the epithelium is a fairly consistent finding. Many authors have isolated bacteria from the stratum corneum or from under the exfoliations. Ulcerations in the gastrointestinal tract in Ritter's disease have been reported by Kendall and Aegerter,[31] Guy and Cohen,[22] and Neff.[39] In Leiner's disease acute congestion, associated with catarrhal changes in the intestinal mucosa, seems to be a consistent finding. Frequently mentioned for both diseases is dilatation and sometimes hypertrophy of the cutaneous vessels. Others have suggested that a diffuse peripheral vascular lesion may be the underlying cause of Ritter's disease. Severe myocardosis and fatty metamorphosis of the liver are not infrequent in both.

CASE REPORT

Clinical History.—The patient, a male infant, was born spontaneously on Jan. 2, 1941, and weighed 8 pounds, 2½ ounces at birth. The mother had received prenatal care; the delivery took place in the hospital. The child was breast fed (as are most cases of Ritter's and Leiner's diseases) and did well for the first days of life. He then developed a small reddish lesion on the chin which healed rapidly before discharge from the nursery. He had two liquid stools on the eighth day of life. At the age of 3 weeks, the child was readmitted with the history that at the age of 17 days he had developed diarrhea and the next day had vomited. At the time he developed an abscess at the base of the spine which discharged blood and pus.

On admission to the Pediatric Service* of Temple University Hospital, he appeared acutely ill. The patient was dehydrated. There were crusting lesions on the lips, the eyelids, and the forehead; there was a purulent conjunctivitis from which *Streptococcus hemolyticus* and *Pseudomonas pyocyanea* were isolated.

The child was given parenteral fluid for two days with cessation of the vomiting and the diarrhea. Sulfathiazole was given for six days after admission but was stopped because of the recurrence of the projectile vomiting. The sulfathiazole level at that time was 3.4 mg. per 100 c.c. of blood. The patient received 10 drops of halibut oil daily and 25 mg. of cevitamic acid. On the tenth day after admission and 48 hours after sulfathiazole was discontinued, his general condition became worse. He developed a macular rash. The temperature rose and oscillated between 101 and 102° F. Two days later the maculopapular rash faded and the child became diffusely red. The spleen was enlarged. The lower extremities became edematous. During all of this time his appetite remained normal.

At this period the blood picture changed. The count had been normal except for an unexplained eosinophilia of 9 per cent. On the tenth day the leucocyte count

*We are indebted to the Pediatric Department, under the direction of Dr. W. E. Nelson, for the clinical history, and to Dr. Nina Anderson for valuable criticism and suggestions.

had risen to 15,650, the neutrophiles had dropped from 73 to 58 per cent with a corresponding increase in the lymphocytes and an eosinophilia of 24 per cent.

The skin became leathery. On the fifteenth day the temperature began to spike. The patient developed spasticity of the legs and had three convulsions. The serum calcium was found to be 5.5 mg. per 100 c.c. of blood. The latter symptoms yielded to calcium medication. The baby now had the appearance of an old man, and the skin began to desquamate: there was no suppuration of the uncovered areas. Nikolsky's sign, which was checked repeatedly, was negative. Other interesting laboratory findings were a carbon dioxide combining power of 25 volumes per cent, which did not respond to medication and which was 38 volumes per cent just before death. The icterus index was 38; van den Bergh's test was strong, direct, and delayed, with 3.3 mg. bilirubin. The spinal fluid was xanthochromic. The calcium was 5.5 mg. per 100 c.c. of blood, with an inorganic phosphorus of 2.9 mg. per 100 c.c. of blood and a phosphatase of 3.8 Bodansky units. These corresponding low findings are difficult to explain in the light of our present knowledge and warrant further investigation. The blood Wassermann reaction was negative. The urine analysis on admission and at all times during the disease showed traces of albumin, leucocytes, and occult blood.

Autopsy.—Anatomic description (five hours post mortem): The body was emaciated, parboiled, and dehydrated; the skin, desquamating. There was some exfoliation under the arms and on the back which was definitely absent before death. The eyes were edematous and almost closed. At the base of the spine there was an area about 1 cm. in diameter which was swollen, the center of which was formed by a sinus tract. It appeared to undermine the muscles. It contained no pus at the time of autopsy.

The other positive findings at autopsy were: a localized, fairly soft yellow area, 1.5 cm. in size, in the upper lobe of the right lung. On culture, this yielded *Staphylococcus aureus* hemolyticus. The heart weighed 20 Gm., and the myocardium was pale but firm. The liver weighed 290 Gm., was congested, and there was bile stasis. The gall bladder was distended and measured 7 by 2 cm. It was pale, edematous, and contained a colorless fluid which, on pressure, flowed out freely into the duodenum. The spleen weighed 13 Gm. and was congested. The pancreas was surrounded by edematous fatty tissue. On section it felt hard and fibrous. Grossly, the kidneys were negative. The stomach mucosa was studded with numerous petechial hemorrhages. The pylorus and duodenum were edematous, and the lumen was barely visible, though a 1 mm. probe could be passed through. The reduction of the lumen by edema explained the projectile vomiting which this child presented both early and late in the disease. The intestinal tract was congested throughout, but no areas of ulceration were grossly demonstrated in any portion. The stools were pale yellow and foamy.

Head: The bregma fontanel was depressed. The brain was edematous and tinged with bile.

Bacteriology:

ANTE MORTEM: Repeated blood cultures were negative. Stool cultures were negative for dysentery and hemolytic streptococcus. Spinal fluid, two days before death, contained pathogenic *Staph. aureus* hemolyticus and was positive for occult blood.

POST MORTEM: Hemolytic *Staph. aureus* in pure culture was found in the blood. The suppuration from the eye yielded, both before and after death, hemolytic streptococcus, *Staph. aureus*, and diphtheroids. The nasal and the peritoneal cultures both showed *Staph. aureus* hemolyticus and *Ps. pyocyanea*. A culture taken from beneath the skin of the axilla showed no growth. From beneath the skin of the back and the side, *Staph. aureus* hemolyticus was isolated.

Histopathology: The skin presented hyperkeratosis accompanied by desquamation, leaving the stratum granulosum almost intact (Fig. 1). The Malpighian layer

was hypertrophied, and the rete pegs were quite prominent. The sweat and sebaceous glands were well developed. Deep in the derma they appeared to merge into large clear cells (Fig. 2). These cells were elliptical to round in shape and were closely packed together. Their cytoplasm stained pale pink with H and E, pale green to

Fig. 1.—Skin. Note the persistence of the stratum granulosum (Masson's stain ×170).

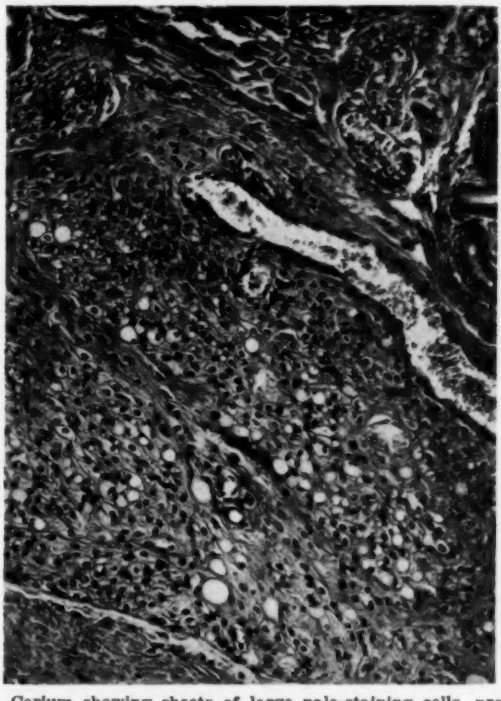

Fig. 2.—Skin. Corium showing sheets of large pale-staining cells, probably atypical embryonic fat cells (H and E stain ×170).

colorless by Masson's stain. It was mostly finely granular but frequently contained droplets and even suggested foam cells. Sudan III stain revealed the presence of a few fat droplets, but it did not account for all the vacuolated spaces found in the cells. Nile blue sulfate stain did not give any additional information. The nucleus was central, ovoid to round in shape; the metachromatic granules stained deeply but were delicate in structure. These cells were so numerous and their appearance was

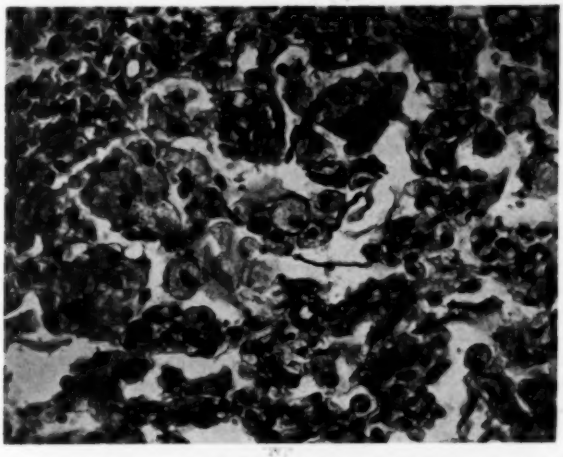

Fig. 3.—Lung. Illustrating accumulation of large lipoid laden phagocytes in pulmonary alveoli (H and E stain ×410).

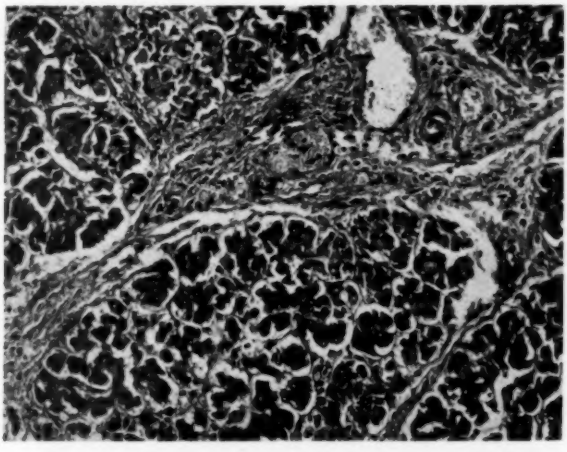

Fig. 4.—Pancreas. Note interlobular and interacinar fibrosis with some mononuclear infiltration (H and E stain ×170).

such in certain sections as to resemble tumor cells. These cells were probably embryonic fat cells but not characteristic ones. The slides have been submitted to several other pathologists and they also were at a loss to identify these cells with any certainty. Throughout the derma many delicate, congested capillaries were found. Sometimes these were so closely woven together as to suggest a vascular neoplasia but careful study did not confirm this. Many small cocci and short round

bacilli were identified in the deeper layers of these cells where localized areas of necrosis were found. Surrounding these were some round cells, a few phagocytes, and occasional plasma cells. Except for some round cells below the rete pegs, the skin was relatively free from cellular infiltration. In the tissue removed from the sinus tract, no surface epithelium was seen, and the lining consisted of muscle bundles free of any inflammatory or degenerative processes.

The *heart* showed some edema and Zenker's degeneration.

The *lungs* presented moderate emphysema, congestion, and occasional small hemorrhages. The alveoli contained numerous phagocytes filled with large fat droplets (Sudan III stain), presenting the picture similar to that of lipoid pneumonia (Fig. 3). Besides these fat droplets there were large phagocytized pink-staining hyalin bodies present in some of the cells. There was also a small infarction surrounded by hemorrhage and bacterial colonies.

The *liver* was congested, edematous, and showed bile stasis.

The *gall bladder* wall was reduced to a thin layer of tissue in which little of the histologic structures could be made out. Several enlarged *lymph nodes* removed from this area showed reticular hyperplasia. A large vessel which had been removed with the tissue was cuffed by an unusual mass of eosinophiles. This was the first and only indication of eosinophilia encountered as compared to the high eosinophile blood count noted during the course of the disease.

The *spleen* was extremely congested and contained some fat laden cells in the sinuses. The vessels were frequently cuffed by plasma cells.

The *pancreas* revealed an interesting picture of interstitial fibrosis, which for the most part did not involve the islands of Langerhans or the acini. There was also a mild inflammatory reaction suggestive of an early pancreatitis (Fig. 4).

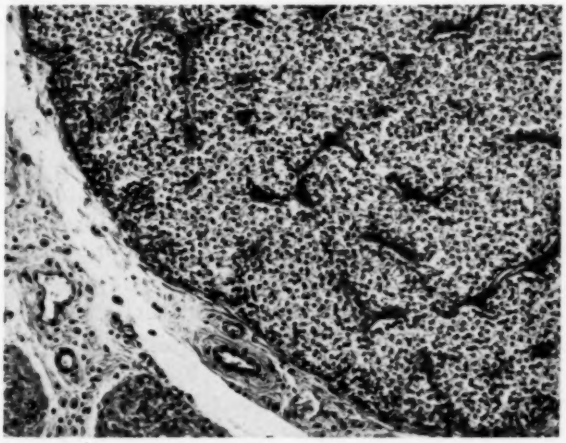

Fig. 5.—Part of parathyroid. Clear cells as seen in three of the four parathyroids (H and E stain ×170).

The *kidneys* showed a moderate nephrosis, and the vessels were congested.

The *adrenals* were markedly congested, most prominently at the junction of the cortex and the medulla. The glomerular layer was reduced to one to two layers of cells with a corresponding increase in the fasicular layer. In the cortex some large fat-laden cells, not of adrenal origin, were again encountered.

The *stomach* showed capillary congestion. The *pylorus* and *duodenum* showed marked edema with hyperplasia of the mucosa and secretory activity. The remaining portion of the gastrointestinal tract showed remarkable congestion. The

capillaries of the mucosa especially were so distended that one marveled that rupture had not occurred. The supportive stroma was infiltrated by plasma cells, round cells, a few neutrophiles, and an occasional eosinophile.

The *bone marrow* was normally active, but occasionally a large clear vacuolated cell was encountered.

The *pituitary* and *thyroid glands* showed nothing of pathologic significance. The *thymus gland,* which was grossly negative, very unfortunately was lost somewhere in the procedure of fixation. The four *parathyroid glands* were fortunately removed. One of these was normal and adult in type. The fat cells were normal. The other parathyroids were all formed by small clear cells but there was no tendency to acinar arrangement except in one tiny area. These parathyroid glands were more like those found in the premature infant than in the 3-week-old child[12, 29] (Fig. 5) (no fat cells were present).

The *brain* sections showed a marked congestion with hemorrhage and a mild encephalitis.

DISCUSSION

Clinically, this case was difficult to classify. The absence of Nikolsky's sign, the desquamation, the parchmentlike skin, the noninvolvement of the feet and the hands, the occasional periods of cyanosis, and the spasticity of the lower extremities were all in favor of the diagnosis of Leiner's disease. Histologically, the conservation of the stratum granulosum, the well-developed epidermis, and the accentuation of the rete pegs likewise suggested Leiner's disease. On the other hand, the absence of seborrhea of the scalp, the ulceration on the back, the presence of deep necrotic subcutaneous lesions, and the mildness of the inflammatory cell infiltration were in favor of Ritter's disease. The high icterus index and the albuminuria have been mentioned by Lindberg[36] in a typical case of Leiner's disease with seborrhea of the scalp and desquamation. The eosinophilia, as Ryan and Goldman[47] justly remark, is not unusual in a general dermatosis. A review of the literature and a careful consideration of this case led us to the belief that the symptoms in these three conditions may merely be varying clinical manifestations to a greater or a lesser degree of a single disease with a common underlying cause. In support of this contention, we find that Sutton and Sutton[57] consider the terms pemphigus neonatorum, Ritter's disease, and Leiner's disease as probably synonymous; they state that they do not believe the latter to be an entity. This study supports that concept.

The history of an apparently normal pregnancy, a normal delivery, and a healthy newborn child is quite typical of these cases. Yet, it seems significant that only certain children contract the disease while others likewise exposed to infection should escape it. Considering the increasing attention which has been given to prenatal care, it is rather surprising that so little has been done to correlate the condition of the mother during pregnancy with that of the child at birth, especially in respect to its adaptation to its new environment. Heredity and congenital anomalies of the skin (though never demonstrated in these cases) have been too generally accepted as the underlying cause. Though it is possible that these factors may be causal in certain cases, the majority

of cases cannot be so easily explained. Few chemical studies have been made on both the newborn infant and on the mother during the immediate postnatal period.

It is true that some of the symptoms, such as the hypocalcemia, may be due to an infection of long standing, but in most of these cases the course of the disease, when fatal, is extremely rapid so that chronicity plays no part. It is interesting that Sinclair[54] has shown that fetal rat parathyroids are stimulated by a subnormal maternal calcium or by an excess of maternal phosphorus and are depressed by an excess of parathyroid hormone from an enlarged maternal gland or by an excess of maternal calcium. Patt and Luckhardt[42] state that decalcified blood which has been perfused through a thyroid-parathyroid preparation, when injected intravenously into the blood of dogs, increases their serum calcium and, in most instances, increases the serum inorganic phosphorus in almost the same magnitude.

In our patient the blood contained 5.5 mg. per cent of calcium per 100 c.c. of blood and 2.9 mg. per cent of inorganic phosphorus per 100 c.c. of blood. The symptoms of calcium deficiency responded to treatment, and the blood phosphorus rose to 5.6 mg. per cent.

Clear cells could be demonstrated histologically in three of the four parathyroids, although what their exact significance was we hesitate to speculate about at the present time.[12, 29] In animals low serum calcium may present different symptoms. The nervous phenomena may be overshadowed by trophic disturbances, such as eczema, loss of hair, a roughened coat, and profound cachexia.[66] Clinically, trophic disturbances of the nails and spasmophilia are described by Leiner in his cases.[33] Experimental observations on animals appear to be of sufficient interest to warrant a thorough investigation of the serum calcium and serum phosphorus and phosphatase concentrations in mother and in child at the time of birth.

In attempting to correlate some of the clinical and pathologic findings with disturbed mineral balance noted in certain cases, the possibility of vitamin deficiencies should not be overlooked. Hypocalcemia and intestinal dysfunction interfere with vitamin absorption[1, 19, 25] which, in turn, is frequently followed by edema. Kussmaal, as cited by Zondek,[66] found gastric dilatation accompanying a pyloric stenosis. The pyloric stenosis found in our case at necropsy was interpreted as the consequence of a pronounced edema rather than that of an organic congenital stricture. The pulmonary edema, congestion, and hemorrhage noted at post-mortem also could be explained, at least in part, as a vitamin deficiency. Even the relative lymphocytosis is not an uncommon finding in vitamin deficiency.

Another feature which requires further investigation is the apparent profound disturbance of the lipoid metabolism in these cases. This has been described for Ritter's disease by Cailliau and Fleury[10] and by Nishinoiri.[41] Curious xanthomatoid cells were found in our case histo-

logically in the deeper layer of the skin, in the lymph nodes and in the lungs. Furthermore, there was a diminution of the thickness of the glomerular layer and a corresponding increase of the fascicular layer of the adrenal cortex in both our patient and in those of the last-cited authors. The presence of fibrosis in the pancreas makes us feel that the process is not one of recent postnatal origin, but rather that it may date back to some period of intrauterine or fetal life.

In some of the reported cases good results were obtained clinically by the use of cod-liver oil alone,[60] by riboflavin alone,[60] or by the two in combination. In other cases a high protein, low fat, and low carbohydrate diet proved helpful,[26] and in others a staphylococcus vaccine was a valuable therapeutic adjunct. Some cases clear up spontaneously,[23] probably as the infant adapted his physiologic response to his new environment.

Dysfunction of the endocrine glands has been long associated with skin disease in the adult,[24] and lately this has been alluded to in Ritter's disease.[9] Vitamin deficiency seems to go hand in hand with it. It is well known that pregnancy puts on the endocrine system of the mother a great demand to which she must adapt herself. Of her physicochemical status at the time of delivery, in correlation with that of her child, we know very little. It seems entirely logical to expect differences in the capacity of the newborn infants to adapt themselves to their new environment since each is dependent to a very considerable degree on how well he was equipped for this experience during his intrauterine existence.

SUMMARY

1. A case of skin disease in an infant is presented with the clinical and the post-mortem findings.

2. A discussion of the relation of pemphigus neonatorum, Ritter's disease, and Leiner's disease is presented, and consideration is given to the possible underlying causes.

I am indebted to Dr. E. S. Gault for the microphotographs which appear in this paper.

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THE Rh FACTOR AND ITS IMPORTANCE IN TRANSFUSION FOR THE ANEMIAS OF ERYTHROBLASTOSIS AND OTHER CAUSES

Case Reports

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RECENT studies have shown that the Rh factor is of considerable importance clinically by virtue of its capacity to induce isoimmunization. It is now clear that this can be brought about by either one of two ways: (1) repeated transfusions of Rh– patients with Rh+ blood and (2) pregnancy in Rh– mothers with Rh+ fetuses.

Levine and Stetson[1] were the first to suggest isoimmunization by blood factors in the fetus as the origin of maternal atypical agglutinins, which were held responsible for a hemolytic transfusion reaction occurring after the first transfusion. Subsequent studies revealed that in this group of cases, i.e., intragroup transfusion reactions at the first transfusion associated with pregnancy, there was a high incidence of abortions and also stillbirths and neonatal deaths which later could be shown to be due to erythroblastosis fetalis.[2-4] Since the specificity of the atypical agglutinins in the blood of these women ran parallel to the specificity of the experimentally produced serum of Landsteiner and Wiener[5, 6] (rabbit or guinea pig antirhesus blood immune serum) the terms Rh and anti-Rh were applied also to the factor in the blood of the fetus and to the corresponding agglutinins produced by the mother.[2-4]

These observations led to the description of the pathogenesis of erythroblastosis fetalis. Actually, the only mystery of this well-known clinical condition lay in the origin of the intrauterine hemolysis. The statistical data indicated that in 90 per cent of all cases the mother is Rh–, the fetus and the father are Rh+.[4] The resulting isoimmunization is indicated also by the demonstration of anti-Rh agglutinins in about 50 per cent of the Rh– mothers. It is the continuous intrauterine passage and action of the anti-Rh agglutinins on the susceptible Rh+ fetal blood which is the source of clinically suspected hemolysis of fetal blood.

A number of practical applications of these findings were pointed out by Levine and his co-workers. In the first place, the anti-Rh agglutinins were found to behave like warm agglutinins.[7, 8, 1] In contrast to the action of anti-A or anti-B, human anti-Rh agglutinins frequently give stronger

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reactions after incubation at 37° C. than at lower temperatures. Hence it was suggested that in addition to the selection of an Rh– donor for an Rh– patient, the mixture of patient's serum and donor's cells be incubated at 37° C. for about thirty minutes and then centrifuged at low speed.[9, 10] Under these conditions the cross-matching will detect incompatibilities due to finer differences within the Rh group.[11]

Second, a laboratory test is available to confirm or to establish the clinical diagnosis of erythroblastosis fetalis. In 90 per cent of these cases the mother will be Rh– in contrast to a value of 15 per cent Rh– in a random population.[4]

Third, 90 per cent of all intragroup transfusion accidents following repeated transfusions in male or female patients occur in Rh– individuals. Indirect evidence for this view can be obtained from the statistical data on the series of mothers of erythroblastotic infants, and it is further supported by the result of reports of Wiener,[12, 13] Diamond,[14] and Vogel, Rosenthal, and Levine.[15] In short, the Rh factor is a good antigen in man either by pregnancy or by repeated transfusions.

Finally, Katzin, Vogel, and Levine[16] pointed out that in view of the susceptibility of the Rh+ fetal blood to the action of maternal agglutinins, Rh– blood should survive in the circulation of the erythroblastotic infant.[4, 11] Hence these workers recommended the use of Rh– donors to combat the severe anemia in the surviving infant. In a small number of cases the response to the use of Rh– blood has been most dramatic.

The significance of these four clinical applications is seen in a description of the following cases recently observed at the Strong Memorial and Rochester Municipal Hospitals.

Tests were carried out in six cases of erythroblastosis fetalis proved by post-mortem examination and thoroughly evaluated. The following observations were recorded: (1) all the mothers had more than one pregnancy; (2) in each instance, blood of the father and mother were tested; (3) those surviving siblings available for blood examination were also tested; and (4) in all but one instance, the mother was Rh– and the father was Rh+. In this case (No. 6) both parents were Rh+.* In the small group of Rh+ mothers it is assumed that still other blood factors such as A, B, Hr, or still finer differences within the Rh group may be responsible for the isoimmunization.[4] These findings are summarized in Table I.

The obstetric histories reveal strong familial tendency in some (Families 1, 2, 4, and 5). In two families (3 and 5) some of the surviving children are Rh– so that their fathers must be heterozygous, i.e.,

*In the exceptional case, No. 6, the father's blood has the dominant property A which is absent in the mother's blood. Should the affected infant belong to group A, specific isoimmunization may possibly occur. The Rh+ series of mothers of erythroblastotic infants is discussed in previous papers.[4, 11]

TABLE I

ERYTHROBLASTOSIS CASES PROVED BY AUTOPSY

FAMILY	PARENTS	BLOOD GROUP	ANTI-RH 1, 2	ANTI-RH 1	ANTI-RH 2	HISTORY
1	F	O	+	+	+	Four pregnancies; two siblings L & W, one died EBF, last child had EBF, now L & W—had splenectomy at age of 42 hours
	M	O	0	0	0	
2	F	A	+	+	+	Eight pregnancies; two died from EBF
	M	A	0	0	0	
3	F	O	+	+	+	Two pregnancies; first child is Rh–, second child died from EBF
	M	O	0	0	0	
4	F	A	+	+	+	Thirteen pregnancies; first six children L & W, seventh died with jaundice, last four diagnosed as EBF
	M	A	0	0	0	
5	F	O	+	+	+	Seven pregnancies; 5 L & W, two of whom are Rh–; two died from EBF
	M	O	0	0	0	
6	F	A	+	+	+	Three pregnancies; two L & W, third died from EBF
	M	O	+	+	+	

F, father; M, mother.
L & W, living and well.
EBF, erythroblastosis fetalis.
The three varieties of anti-Rh sera are now designated as anti-$Rh_{1, 2}$, anti-Rh_1 and anti-Rh_2. (Levine, P.: Science **96**: 452, 1942.)

of the genotype Rhrh. Accordingly the outlook for future normal children in such matings is 50 per cent. In genetic crosses of heterozygous (Rhrh) father × Rh– mother (rhrh), 50 per cent of the offspring should be Rh+ and capable of inducing isoimmunization, but the remaining 50 per cent should be Rh– and therefore not susceptible to erythroblastosis fetalis.[4, 11]

CASE REPORT

CASE 1.—This case is presented as illustration of the value of the suggestion of Katzin and co-workers; i.e., the use of Rh– blood for transfusing the affected infant in combating the increasingly severe anemia which is so characteristic of erythroblastosis fetalis.

History.—Mrs. P., 28 years of age, had one normal child by her first husband, and delivered a presumably normal infant on Aug. 26, 1941. Jaundice was first noted in the infant at the age of 7 days. On the eighth and ninth days of life the jaundice became more intense, and enlarged spleen and liver were noted. At this time, the question of a diagnosis of erythroblastosis fetalis was considered. Accordingly, Rh tests were carried out with the use of potent human anti-Rh sera. The results were as follows:

Father, group O—Rh positive
Mother, group A—Rh negative
Baby, group A—Rh positive—

Although this was ample evidence to establish the diagnosis of erythroblastosis fetalis, still further proof was the demonstration of moderately potent anti-Rh agglutinins in the mother's serum. This serum agglutinated intensely the red cells of the father, the infant and other bloods known to be Rh+.

The anti-Rh agglutinins were detected by the procedure recommended by Levine.[4, 10] Since the same method is also useful in the direct cross-matching test for the selection of a compatible donor, a brief description is indicated. The test is carried out as follows:

1. To a series of test tubes add two capillary drops each of 10 washed blood suspensions (2 per cent) of group O, of which two should be Rh–.

2. To each tube add two or more drops of the serum to be tested for anti-Rh agglutinin content.

3. Incubate about sixty minutes or longer in a water bath of 37° C, with occasional shaking.

4. Readings may be made at this time either by observing the character of the sediment or by centrifuging at very low speed and very gentle resuspension of the sedimented cells. In either case the character of the sediment is very important; if loose and irregular in outline, clumping should be grossly visible; a round and firm sediment indicates the absence of agglutination, and this can be confirmed by microscopic observation. The presence of weak atypical agglutinins should always be confirmed by microscopic examination.

Titration of the anti-Rh agglutinin content of this patient's serum with the use of the centrifuging method revealed a titer of 1:32 to 1:64.

On the ninth day of life, the infant's condition was very serious and further therapy was considered. The infant had already received three transfusions of the mother's blood, but this was done prior to the demonstration of anti-Rh agglutinins in the mother.

Thus the hemolytic process was still progressing, not only because of the continued action of maternal agglutinins probably stored during the fetal period, but because of the transfused maternal anti-Rh agglutinins. Although the mother's transfused Rh- blood cells are expected to survive in the infant's circulation, the use of this mother's blood was contraindicated because of its anti-Rh agglutinin content.* Accordingly, the suggestion of Katzin and co-workers was carried out and a transfusion of Rh- blood from another donor was given on the eleventh day. The sudden increase in red cell count and hemoglobin was truly remarkable.

The subsequent drop on the twelfth day and later indicated that the infant's own Rh+ blood was probably still undergoing destruction. During this interval, the infant's life was maintained because of a sufficient quantity of foreign Rh- cells. The value of this measure lies in the fact that transfused compatible blood should survive in the circulation for a period of from three to four months,[17-19] after which interval the hemolytic process will have ceased. As a result of these several transfusions with Rh- blood, the infant's blood apparently seemed to behave as though it were Rh- because it now failed to react with standard anti-Rh sera, although at birth the blood reacted intensely. Actually, microscopic examination of the mixture of anti-Rh serum and infant's cells showed occasional clumps made up of a small number of cells, but the greater portion of the microscopic field contained nonagglutinated Rh– cells. In other words, the infant's blood consisted of a mixture, the far greater part of which was made up of the surviving Rh- transfused blood, while the occasional clumps consisted of the baby's own characteristic Rh+ blood cells which were still susceptible to destruction.

The child was finally discharged after three weeks with a red blood count of 4.01 million; hemoglobin, 12 Gm. per 100 c.c.; and icteric index, 11. At the age of 1 month the infant was seen at home and agglutination tests at this time revealed that the circulating red blood cells were almost exclusively Rh-. During the next five months we were unable to contact the patient. Finally, at the age of 6½ months additional tests were made. After this long interval all the foreign Rh- blood

*A similar case observed by Vogel and Levine was cited recently.[4]

TABLE II

AGE	TRANSFUSION (C.C.)	R.B.C.	HB.	ICTERIC INDEX	TEST WITH ANTI-RH SERA
8 days	90* (A.M.)	2.3	9.5		
8 days	80* (P.M.)	2.19	7.0	48	+++
9 days	105*	1.8	7.5		
10 days	150	2.91	7.0	60	
11 days		3.95	12.0	48	- except for occasional clumps
12 days		6.58	15.5	30	
15 days		3.85	16.0	24	- except for occasional clumps
19 days		4.01	12.0	11	
28 days		4.2	14.0		
		Six-Month Interval			
7 months		5.55	14.8		+++

*Indicates mother's blood used for transfusion. The fourth transfusion (150 c.c.) on the tenth day was from a male Rh- donor.

had been replaced by the infant's own characteristic Rh+ blood, as indicated by strong reactions with standard sera. At this time, the red blood count and hemoglobin were 5.5 million and 14.8 Gm., respectively. The icteric index was 6.

A similar series of events were observed by Levine[20] and co-workers in several other affected infants who were transfused with Rh- blood. Unless one is aware of previous transfusions with Rh- blood, Rh tests of the affected infant may be misleading since the small number of clumps characteristic of the still surviving but susceptible Rh+ infant's blood may be readily overlooked because of the preponderance of transfused Rh- blood.

In view of these considerations it is certain that this infant would never have survived the hemolytic process had it not been for the transfusion of Rh- blood. The results in this case fully confirm the observations of Katzin, Vogel, and Levine based on a small number of erythroblastotic infants.

It must be emphasized that had the mother required a transfusion following the delivery, only Rh- blood could be given. The transfusions of Rh+ blood in cases of this sort resulted in severe and even fatal transfusion reactions obviously attributable to the presence of anti-Rh agglutinins in the serum of the mother. Actually, intragroup transfusion reactions may occur even in the absence of demonstrable agglutinins but only in cases where isoimmunization has occurred, either by pregnancy or by repeated transfusions.[10, 13]

CASE 2.—This case report deals with an intragroup transfusion reaction in an Rh- patient who was immunized by repeated transfusions of Rh+ blood. Although this patient was an adult, similar instances in children were reported by Diamond[14] and Vogel, Rosenthal, and Levine.[15]

Case History.—The patient, a 42-year-old married woman, was observed in the clinic for a period of one and one-half years for cirrhosis of the liver which was progressively becoming worse. In addition to the severe jaundice in which the icteric index ranged from 80 to 165, there was a profound anemia. The red count remained at a level of two to three million cells per c.mm., with a hemoglobin value of from 9 to 10 Gm. The treatment of the patient consisted mainly of repeated transfusions, for this procedure proved to be most beneficial in lowering the icterus index, combating the anemia, and bringing about a favorable clinical response in the patient. Suddenly, however, the patient had violent and almost fatal reactions to any blood of her own group, even though the very same donors were previously used uneventfully.

In the course of investigating the cause of the severe transfusion reactions, it was found that the patient was Rh- and that two donors previously used for un-

eventful transfusions whose blood now caused severe reactions were Rh+. The interval between the two transfusions with the same donor was two months. Each of the six donors previously found compatible was now incompatible with the patient's serum and each one was Rh+, as indicated by tests with potent anti-Rh sera. Subsequently, four successful transfusions were carried out with Rh- donors and in each instance there was some rise in hemoglobin and red cell count.

Incidentally the anti-Rh agglutinins in this case were not very strong and associated with it was a marked pseudoagglutination. The confusing effects of this phenomenon were avoided by carrying out the tests in test tubes and not on glass slides. For the selection of Rh- donors, potent anti-Rh sera were employed but not the patient's serum. Once Rh- donors were selected, their blood was tested at 37° C. with the patient's serum as indicated above.

COMMENT

These two cases illustrate the significance of the four above-mentioned clinical applications resulting from the recent work on the importance of the Rh factor. In any patient to be transfused, the possibility of previous isoimmunization by pregnancy, by transfusion, or a combination of both factors, should be kept in mind. It is important to investigate all transfusion reactions to determine whether or not the Rh factor is involved. Only a very small number of transfusion reactions will remain unsolved if all Rh- patients receive Rh- blood. In addition, the modified warm compatibility test should be carried out in order to detect finer degrees of specificities of various anti-Rh sera.

SUMMARY

1. In five out of six cases of erythroblastosis fetalis verified by autopsy findings, the mother was Rh- and the father and affected infant were Rh+.

2. The survival of transfused Rh- blood and the continued destruction of the erythroblastotic infant's Rh+ blood is indicated by the temporary change of its Rh reaction from positive at birth to negative after transfusion with Rh- blood.

3. The antigenicity of the Rh factor by repeated transfusions was demonstrated in one case.

4. For detection of anti-Rh agglutinins, the method of choice is incubation of patient's serum and Rh+ blood suspension at 37° C.

5. Rh- patients should be tranfused with Rh- blood, if the modified compatibility test is satisfactory.

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MORTALITY IN ACUTE STAPHYLOCOCCAL EMPYEMA IN INFANTS AND CHILDREN

A Study of Thirty-Three Surgically Treated Patients

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INTEREST in staphylococcal infections is heightened at the present time by the recent appearance of certain biologic preparations as potential adjuncts to the therapeutic armamentarium against that organism. It seems particularly worth while at this time, therefore, to review our past experience with acute staphylococcal empyema in infants and children as a base line study by which the effectiveness of newer biologic bacteriocidal agents such as penicillin and gramacidin may subsequently be judged. This paper presents mortality data on thirty-three patients under 13 years of age with acute staphylococcal empyema surgically treated during the past ten years at the Children's and Infants' Hospitals.

In analyzing our patients it was at once apparent that in some of them a clinically identifiably septicemia was present at the time the empyema was first recognized, while in others, the pneumonic and Pleural infections were the only foci which could be demonstrated. To establish the prognostic significance of this presence or absence of multiple foci of staphylococcal infection, we have divided our patients into two groups. In the first group, termed "uncomplicated," no other focus of infection was found at the onset of the empyema. In the second, "complicated," group one or more other localized sites of infection was present associated with the empyema.

In the "complicated" group, a considerable variety of associated lesions was found. Four had suppurative otitis media, three bronchiectasis, one laryngotracheobronchitis, one primary osteomyelitis of the rib, one septic conjunctivitis, and one cellulitis of the leg associated with multiple foci of osteomyelitis, septic knee, and pericarditis. In these patients it was felt that a widespread infection was present, and blood stream invasion was presumed to have occurred. In many instances this bacteriemia was proved by positive blood cultures.

Fig. 1 presents the age incidence and mortality rate of our two groups of patients. Two very striking facts, we feel, appear from this chart. First, *the incidence of staphylococcal empyema was preponderantly greatest in the first year of life, and, indeed, in the first three months of life.* Thus, of our thirty-three patients, twenty-two were less than 1 year old, and twelve were less than 4 months old. The remaining cases were dispersed throughout the childhood years. Age appeared to

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have a bearing on the presence or absence of complications, as complicated cases occurred in greater numbers among the older children, while the uncomplicated cases predominated in early infancy. That the difficulty of diagnosis of complications in infancy is greater must be admitted, and thus complicating foci may have been missed in some of these individuals. It is possible, therefore, that the relation of age to the presence or absence of complications may be more apparent than real.

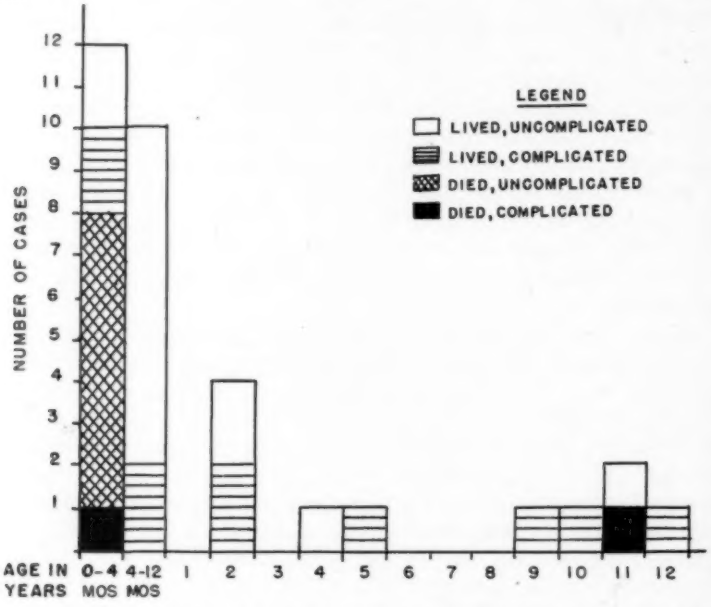

Fig. 1.—Mortality in relation to age and to presence of complicating foci of infection.

Second, *the mortality rate appeared to be almost entirely dependent on the age of the patient, and the dividing line is remarkably sharp at 4 months of age.* Thus, of our twelve patients less than 4 months old, eight died, a mortality of 66.7 per cent. On the other hand, of twenty-one patients of 4 months or older, only one died, a rate of 4.8 per cent.

We repeat this data in simplified form in Table I for emphasis.

It would appear that the presence or absence of complications had little relation to eventual outcome. Surprisingly enough, the patients in the complicated group, who were thought to represent the sicker individuals with widespread infection and bacteriemia, carried no greater (indeed even a lower) mortality rate than the complicated ones. It seems paradoxical to say that the patients whose empyema is already complicated have a better chance of survival than those uncomplicated but such has been our experience. Table II presents this data.

TABLE I

MORTALITY IN RELATION TO AGE IN STAPHYLOCOCCAL EMPYEMA IN INFANTS AND CHILDREN

AGE	TOTAL CASES	DIED	SURVIVED	MORTALITY (%)
Birth to 4 mon.	12	8	4	66.7
4 mon. to 12 yr.	21	1	20	4.8

TABLE II

MORTALITY IN RELATION TO PRESENCE OF MULTIPLE FOCI OF INFECTION

TYPE	TOTAL CASES	DIED	SURVIVED	MORTALITY (%)
Uncomplicated	21	7	14	33.3
Complicated	12	2	10	16.6

To understand this seeming contradiction, we must revert again to the element of age. As was shown in Fig. 1, the very young infants were chiefly the uncomplicated patients, while the older individuals more frequently presented complications. One must conclude, we believe, that the presence or absence of multiple foci has no particular relation to the ultimate outcome but that what is more important is the age of the patient. We feel that *age is the single most important factor in relation to mortality,* and this is true whether or not the patient presents evidence of septicemia with multiple foci of infection at the time his empyema is first recognized.

COMMENT

Several reports are available in the literature containing data on the mortality of staphylococcal empyema in infants and children and most authors feel that the mortality is greatest in the group under 2 years of age. However, in most of these reports no detailed age analysis (that is, by months of age) was made. Thus, there are little data in the literature with which we may compare our results, for, in the light of our experience, to discuss mortality in this disease apart from age groups is pointless and misleading. Three reports, however, are of interest in this connection. Hochberg and Kramer[1] present thirty-three cases of patients by ages. In their series of eleven patients under 6 months of age, six died, a mortality of 55 per cent. Of twenty-two patients over 6 months of age, seven died, a mortality of 32 per cent. Farr and Levine[2] present six cases of staphylococcus empyema in patients with four deaths, a mortality of 66 per cent. All four patients who died were 2 years old or less, while the two who survived were 5 and 11 years of age. Thus, in this series, the mortality for patients less than 3 years old was 100 per cent. Reinhoff and Davison[3] present eight patients under 2 years of age, with three deaths, a mortality of 37.5 per cent. However, they do not state the exact age of these patients, so

we do not know if their experience with the very young infant (as contrasted with those 4 months old or more) is similar to ours.

In this report, no attempt has been made to relate mortality to type of treatment, as the latter has remained consistent during the period studied. (All of the patients had surgical drainage, a large percentage had sulfonamide therapy, and some had specific antiserum.) This aspect of the total empyema problem has been recently discussed in a report from this clinic.[4]

We wish to emphasize that the element of septicemia seems strangely unrelated to eventual outcome. Many of our patients with complicated cases were desperately ill. For example, one 2½-year-old child began with fulminating laryngotracheobronchitis due to the staphylococcus, requiring tracheotomy and repeated bronchoscopy to maintain an airway. He subsequently developed bilateral empyema, with spontaneous bilateral tension pneumothorax with underlying pulmonary abscesses. His condition remained precarious for weeks, but his recovery was at last steady and complete. Another child, 10 years of age, began with cellulitis and soft tissue abscess of the leg which spread to the blood stream. In succession osteomyelitic foci in the tibia, mandible, and humerus appeared and were drained. A septic knee and purulent pericarditis were present at the time his empyema was recognized. All the lesions were drained, including the pericardium. His condition was critical for many days and his recovery prolonged, but he recovered entirely except for residual skeletal deformities secondary to his osteomyelitis. A third patient presented a virulent ethmoiditis which progressed to an orbital abscess at the time her empyema was drained. Her recovery was eventually complete.

The markedly higher mortality in early infancy suggests strongly an abnormal pathologic and immunologic response to staphylococcal infection in this age group. That the pathologic response is, indeed, different is suggested by both clinical and pathologic observations. Clinically, it has frequently been found that the mediastinum fails to become fixed, even though the exudate may become thick and fibrinous, and mediastinal shift or flutter may accompany open drainage. At autopsy, an infectious process in the lungs frequently presents a lesion which is patchy but widespread in distribution and is characterized by a hemorrhagic exudation into the alveolar spaces. Abscess formation with walling off may not be present, or, if present, the abscesses are multiple and miliary. Almost all of these patients died in the second and third weeks from the onset of symptoms, and thus their lesions as found at autopsy are relatively young. However, regardless of the reason, the fact is that the hemorrhagic exudative pneumonic process is found more frequently in early infancy, while large abscess formation is more frequent in the older children.[5]

The immunologic pathogenesis of staphylococcal infections in man is poorly understood, irrespective of age, in spite of many diligent and

excellent attempts to elucidate this problem. Rigdon[6] and Longacre[7] have recently reviewed the existing data. It seems clear from these reviews that our knowledge of the immunologic and bacteriologic aspects of pathogenesis in staphylococcus infection is fragmentary and that much of the data is conflicting. There are two studies, however, which bear directly on the problem of differences in immune responses in different age groups, specifically in the very young infant. Kobak and Pilot,[8] using a staphylococcal filtrate to test skin reactivity to intradermal injection, found that 98 per cent of the mothers reacted positively while none of their newborn infants showed positive skin reactions. At 3 months of age approximately 3 per cent of the infants reacted, at 4 months, approximately 5 per cent, while in the succeeding months the percentage rose until at 1 year, 75 per cent of the infants gave positive reactions. Thus it would appear that the newborn infant does not react positively to skin-test doses of staphylococcal filtrate, but that between the fourth and twelfth months the greater majority become positive reactors, while with the same filtrate the mothers reacted positively in 95 per cent of the cases. In this one respect, therefore, we may say that a marked difference has been shown to exist between the neonatal infant and the older infant or adult.

Bryce and Burnet[9] have demonstrated a constant age variation in the titer of antihemolysins (staphylococcal) in the blood serum. They find that at birth the titer is usually high but falls rapidly to almost zero at about the second month, after which it rises sharply again until by the age of 4 or 5 years it approximates the average adult level. It should be noted, however, that there were marked individual variations in each age group. Nevertheless, the average readings seemed to give a definite trend beyond the limit of the inherent experimental variation. Thus, in respect to antihemolysin titers also, we may say that definite differences between the neonatal and older infants or children have been demonstrated.

The interpretation of these data with a view to practical clinical application is, at the moment, impossible. Neither skin testing nor antihemolysin titers have been shown to be a measure of immunity. It is true that such titers tend to increase after toxoid injection and in the presence of active staphylococcal infection. However, the titer often does not increase with staphylococcus infection, and clinical improvement may or may not parallel antihemolysin titers.[6, 7]

In the patients with staphylococcal empyema who have died in infancy, it has been the usual finding at post-mortem examination that the empyema has been adequately drained and the lung has partially or completely reexpanded, but that the hemorrhagic pneumonia has advanced.[5] It is our feeling that the empyema has not been the cause of death in these infants, but that the primary lethal factor has been the progression of the underlying staphylococcal pneumonic process resulting in generalized infection. We feel, therefore, that, although the ade-

quate surgical drainage of the empyema will continue to be a very important aspect of the treatment of staphylococcal empyema in infancy, any future decrease in the mortality in this age group must eventuate from a better and clinically practical understanding of the immune processes involved or the acquisition of therapeutic agents effective against the most basic and lethal aspect of the disease, the underlying staphylococcal pneumonia.

SUMMARY

1. Mortality statistics in thirty-three cases of acute staphylococcal empyema in infants and children are presented.

2. The disease is most common in the first year of life.

3. Age is the single most important factor influencing mortality. From birth to 4 months of age, the mortality was 66.7 per cent. From 4 months to 12 years of age, the mortality was 4.8 per cent.

4. Differences in the pathologic reactions and immune responses have been demonstrated between the very young infant and the older age groups.

5. In the fatal cases in early infancy, progression of the underlying staphylococcal pneumonic process has appeared to be the cause of death. It is suggested that improvement in mortality rates in this age group probably must derive from a more effective therapy of the staphylococcal pneumonia.

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THE USE OF ACETYLARSAN IN THE TREATMENT OF CONGENITAL SYPHILIS IN CHILDREN

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IN A study reported[1] some years ago on the use of acetarsone in the treatment of congenital syphilis, I came to the following conclusions:

1. The effect on the cutaneous lesions, the swelling of the joints in the young infants, the pains and motion of the extremities, the condylomas, and the general enlargement of the glands was remarkable. All of these conditions showed either complete healing or marked improvement.

2. Syphilitic keratitis cleared up as well as could be expected under any other treatment.

3. The hemoglobin content in young children improved in the majority of cases. This was not true in older children.

4. The serologic reaction in young children was reversed in the majority of cases.

5. The spinal fluid in all of our patients gave a negative reaction after the completion of treatment.

6. Bone lesions did not heal very fast.

7. The general health of all the patients showed marked improvement.

These conclusions were confirmed by many writers who followed up their cases in a manner similar to ours.[2, 3, 4, 5]

An opportunity has been presented to us to make a study of a drug which is very similar to acetarsone but which is not given orally but, instead, intramuscularly. This drug is acetylarsan. It is a pentavalent compound containing 21.5 per cent arsenic. It occurs as a white powder freely soluble in water, and is usually administered by subcutaneous or intramuscular injections, although it may be given intravenously. The preparation which is closely allied to, and a derivative of, stovarsol is stated to be p-oxy-acetylamino-phenylarsinate of diethylamine. Acetylarsan is supplied in an aqueous solution containing 23.6 per cent of the compound. It is neutral in reaction, colorless and clear, and contains 5 cg. of arsenic per c. cm.; each cubic centimeter contains 0.25 Gm. of novarsenobillon in arsenic content.

Dosage.—Acetylarsan is given intramuscularly, ½ c.c. for twenty pounds of body weight, which is equal to 0.025 Gm.

Course of Treatment.—Acetylarsan is supposed to be given in courses of nine weeks of treatment, alternated by six weeks of rest, and then repeating the same course again.

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The acetylarsan used in these cases was kindly supplied by Merck & Co., Inc., Rahway, N. J.

In our course no rest period was given and patients usually received from twenty to forty treatments continuously.

Kolmer and Rule[6] have made a study of the trypanocidal and spirocheticidal properties of this drug. When given to rats by intramuscular injections, twenty-four hours after intraperitoneal inoculation with *Trypanosoma equiperdum*, single doses as high as 0.200 Gm. per kilogram were without trypanocidal activity, although the development of infection was restrained for about eight days.

When given to rats by intramuscular injection after intraperitoneal inoculation and the presence of trypanosomes in the peripheral blood, correspondingly large doses were likewise without trypanocidal effects so that it may be stated that single doses equal to the maximum tolerated amounts were without complete trypanocidal effects, although these large doses effectually restrained the trypanosome infections for about a week.

In these particulars acetylarsan was similar to stovarsol. However, Kolmer believes that acetylarsan by intramuscular injections has proved somewhat less spirocheticidal than stovarsol by oral administration.

However, when intramuscular injections were given in rats in doses of 0.020 Gm. or more per kilogram every five days for twelve injections, not only was there produced more rapid healing in testicular lesions, but also about 60 per cent of the animals became Wassermann-negative and yielded lymph gland transfers.

It is evident from the work of Kolmer and Rule that acetylarsan possesses somewhat less spirocheticidal activity by intramuscular injections than stovarsol by oral administration.

According to Lloyd[7] no spirochetes survive in the superficial layers of the primary lesions of acquired syphilis after a period of twenty-four hours following the injection of acetylarsan. In certain cases the spirochetes were killed within six to twelve hours.

The experimental work of Voegtlin and Thompson[8] has demonstrated the rapid elimination of arsenic in the urine and feces of rats following the administration of compounds of the pentavalent group. No exact figures are available of the elimination rate of arsenic during the first twenty-four hours following the administration.

THE TOLERATION OF THE DRUG

This drug seems to be well tolerated by children, as no vasomotor reactions were noticed, nor were there any examples of delayed arsenical poisoning giving rise to late jaundice or exfoliative dermatitis.

In our own series of cases only one patient developed topic symptoms. In Case 10, female, 6 months of age, after six injections of acetylarsan the baby developed a diarrhea and macular rash over face, chest, and arms with hyperpyrexia for nine days. Improvement was gradual and treatment was discontinued with the diagnosis of arsenical dermatitis.

However, it is important to know some of the reactions following this drug and the following have been reported:

1. Hyperpyrexia and malaise.
2. Vomiting some hours after an injection; also nausea and vertigo.
3. Toxic erythematous eruption.
4. Albuminuria.
5. Jaundice.
6. Herxheimer reaction.
7. The most frequent phenomenon complained of is headache. This complaint, of course, would be difficult to elicit in young infants.

RÉSUMÉ OF CASES

We wish to give a brief summary of the cases treated, the patients receiving from sixteen to thirty weekly treatments.

Group I.—In this group eleven patients between the ages of 3 weeks and 1 year were treated. All skin lesions cleared up very promptly, although most of the infants received from twenty to thirty injections.

(a) Serologic reversal was noticed in four out of eleven. The other patients continued to have a positive Kahn test, even when they received from twenty to thirty treatments.

(b) In six infants in whom syphilis was demonstrable roentgenologically before treatment, three showed marked improvement and two showed no evidence of syphilis. In the remaining infants there was still a considerable degree of syphilitic involvement of the bones.

Group II.—This group consists of patients from 1 to 12 years of age.

(a) The secondary lesions which are so common in this period remained unimproved except for a female, 8 years of age, who came to us with a diagnosis of iridocylitis, which was healed after a few treatments.

(b) Serologically the condition of the patients in this group remained positive before and after treatment. However, it is common knowledge that many patients in this group always remain serologically fast, no matter how much treatment is given them. Smith and others have shown that these patients can remain free of symptoms if treated for some length of time, although their Kahn test continues to remain strongly positive.

c) In this group we have a report on one case only where roentgen ray examination before treatment showed indications of congenital syphilis involvement. The condition of this patient remained positive after thirty-six treatments.

DISCUSSION

The use of acetarsone alone by mouth has yielded therapeutic results as far as the usual lesions of early congenital syphilis are concerned. Healing of skin lesions can be demonstrated and the relief of pain can be established in a very few weeks. In 1941 one of us (J. Y.) made a

study of the use of acetarsone in combination with bismuth. When the latter was added to the oral use of acetarsone, fully 80 per cent of the cases showed a reversal of the Kahn reaction. Nearly all clinical conditions improved or healed and, roentgenologically, one could demonstrate marked healing or improvement. The use of acetylarsan in young children apparently can bring about the same results as when acetarsone is used by the oral route. That is, we can show healing in the newborn infant of the simple lesions found in congenital syphilis. However, when secondary lesions are found or when marked bone syphilis is present it is very difficult to eradicate this disease by the use of acetylarsan alone.

CONCLUSIONS

1. Acetylarsan does not seem to bring about toxic results when used in very young children.

2. The Kahn test is not universally reversed in young children, even after a course of thirty treatments. This would demonstrate the necessity of using the drug for a long time in order to bring about serologic reversal in the very young.

3. Roentgenologic improvement of osseous lesions is seen more often in young babies than in older children.

4. Skin lesions and other manifestations in the very young can be improved by the use of acetylarsan.

5. Older children do not respond to the drug alone. There is a possibility that with the aid of bismuth, lesions of late and latent syphilis would be improved or prevented in this manner.

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478 PEACHTREE STREET, N. E.

WHOLE LACTIC ACID EVAPORATED MILK DOES NOT REQUIRE A REFRIGERATOR

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NOW that refrigerators are "frozen," which is not intended as a pun, foods which can be kept at room temperature are necessary, especially for infants who are more susceptible to intestinal infections than are adults. As may be seen in Table I, whole lactic acid evaporated milk* can be left in open dishes at room temperature for three days before becoming infected with molds and for five days before bacteria appear. As the total feeding of evaporated milk made from the usual 13-ounce can* is always consumed by the infant within forty-eight hours, it is obvious that a refrigerator is unnecessary. As Rothey[1] has shown, the lactic acid acts as an antiseptic.

In addition to this advantage of its "keeping" qualities at room temperature, whole lactic acid evaporated milk, which was introduced by Marriott[2] and has been used for all of the infants in Duke Hospital for the past ten years, has the following merits:

Digestibility.—Infants thrive on whole lactic acid evaporated milk, at least as well as they do on breast milk.[3] The incidence of diarrhea, vomiting, and bacillary dysentery is lower in infants fed whole lactic acid evaporated milk than in those receiving any other food.

Safety of Source.—The evaporation process of the whole lactic acid evaporated milk removes the risk of brucellosis (undulant or Malta fever), diphtheria, dysentery, foot and mouth disease, scarlet fever, septic or streptococcus sore throat, tuberculosis, typhoid and paratyphoid A and B fevers, and other diseases which can be spread through dairies.

Safety in Home Handling and in the Infant's Intestine.—The demonstration by Rothey,[1] that dysentery, typhoid, and paratyphoid bacilli, when added in large amounts to whole lactic acid evaporated milk, are destroyed rapidly is an indication of bactericidal power which no other infant feeding process possesses. The antibacterial or lysozyme strength of breast milk is weak in comparison. Sweet milk and powdered milk mixtures, even when boiled in the nursing bottle, can be infected by the

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*The contents of a 13-ounce (390 c.c.) can of unsweetened evaporated milk are poured into a quart jar, previously "scalded" with boiling water, and the empty can nearly filled with boiling water, in which then are dissolved one teaspoonful of lactic acid (U.S.P.) and three level tablespoonfuls of sugar. As soon as this solution is *cold*, it is poured slowly into the quart jar containing the unsweetened evaporated milk while shaking the jar constantly. Although not necessary, it is advisable, in order for the lactic acid to accomplish its full bactericidal effect, that the mixture be kept six hours before being fed in required amounts to the infant. It should not be boiled or pasteurized as it will curdle. Infants of any age can be fed 100 c.c. (100 calories) of this mixture per kilogram of body weight (1½ ounces [45 calories] per pound) in twenty-four hours, divided into four to six feedings. If a child requires more than this amount (one can each of milk and water, a total of 780 c.c., 26 ounces), he also needs solid food.[5]

TABLE I

DAILY CULTURES OF WHOLE LACTIC ACID EVAPORATED MILK EXPOSED IN OPEN DISHES AT ROOM TEMPERATURE

CULTURE MEDIUM	DAYS OF EXPOSURE AND RESULTS OF DAILY CULTURES							
	1	2	3	4	5	6	7	8
Broth	0	0	0	0	+[2]	+[2]	+[2]	+[2]
Dextrose agar	0	0	0	0	0	0	+[2]	+[2]
Blood agar	0	0	0	0	0	0	+[2]	+[2]
Sabouraud's medium for fungi	0	0	+[1]	+[1]	+[1]	+[1]	+[1]	+[1]

[1] *Penicillium glaucum* and Aspergillus.
[2] *Bacillus subtilis.*

mother's hands while attaching the nipple; whole lactic acid evaporated milk, because of its bactericidal activity, cannot readily be infected. This bactericidal action also is useful in reducing the growth of bacteria in the upper intestines which accompanies diarrhea.[4]

Cheapness.—Whole lactic acid evaporated milk is cheaper than practically all other feedings, except breast milk, if it is assumed that breast milk does not cost anything, a premise with which no mother would agree. The cost of whole lactic acid evaporated milk is one-half that of any other infant feeding.

Universal Obtainability.—Whole lactic acid evaporated milk is available everywhere, while in some areas good dairy milk cannot be purchased.

Evaporated milk feedings also have the advantage of simplicity* and of being beneficial in eczema and allergy, as the heating process reduces its antigenic action. The only objections to whole lactic acid evaporated milk are the destruction of vitamins and altered taste. However, all children 8 days to 3 years of age, despite irradiation and regardless of their type of feeding, should receive percomorph or cod-liver oil and ascorbic acid or their equivalents. Some infants dislike whole lactic acid evaporated milk, especially those who previously have been fed with very sweet mixtures, but always, if the physician and mother cooperate, this difficulty can be overcome. In fact, later many of these same children, after they have become accustomed to whole lactic acid evaporated milk, refuse to drink sweet milk—a consummation much to be desired. The addition of flavoring extracts, such as chocolate syrup, improves the taste of evaporated milk, especially for older children and adults. The lead content of canned milk is of no hygienic significance.[5]

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THE USE OF CEREAL-THICKENED FORMULAS TO PROMOTE MATERNAL NURSING

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WHEN complemental bottle feedings are given in conjunction with maternal nursing to compensate for deficits in the supply of mother's milk, infants soon acquire an increasing willingness to take the bottle at the expense of a corresponding decline in the vigor with which they nurse the breast. The resultant continued incomplete drainage of the gland progressively diminishes its production of milk, and it is owing chiefly to these interrelated factors that complemental bottle feedings favor the early discontinuance of maternal nursing.

The consumption of semisolid food in amounts sufficient to compensate for various degrees of inadequacy in the supply of mother's milk usually does not appreciably diminish the vigor with which infants nurse the breast. Consequently, the use of appropriate semisolid foods to the exclusion of complemental bottle feedings has the distinct advantage of favoring the continuance of maternal nursing. Owing to my desire to encourage breast feeding, I have exploited, throughout a period of years, this special superiority of suitable foods of moderately thick consistency over liquid milk mixtures.

This report presents observations on a selected group of fifty-one infants (twenty-three males and twenty-eight females) whose records exemplify my general experience with this special method of feeding. Each of these infants nursed throughout a period of eight months but consistently failed to obtain mother's milk in adequate quantities. Instead of complemental bottle feedings, these babies received a moderately thick preparation composed of farina or oatmeal cooked in equal parts of whole cow's milk and water with 5 per cent cane sugar and a pinch of table salt added to the mixture. This complemental feeding was started routinely on the third day of life, and it was given by spoon in amounts that were varied in accordance with individual desire and need for additional food.

As customarily occurs during initial spoon feedings, these young infants used the tongue to push the semisolid mixture forward out of the mouth, but in a comparatively few days this reflex was replaced by a more mature act of swallowing. After this adjustment was made the babies soon displayed a distinct preference for rapid rather than for slow spoon feeding.

The policy of starting this method of feeding the third day of life had the advantage of acquainting the infants and their mothers with the procedure before they left the hospital. This brief experience gave the

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mothers confidence in the cereal-thickened formula and thus their usual inclination to give bottle feedings to infants who seem to be hungry was counteracted.

Throughout the first few weeks of life the semisolid food was offered immediately before nursing, but after the infants became thoroughly accustomed to the preparation, this order of feeding was occasionally reversed, particularly if the consumption of exceptionally large servings of the farina-milk mixture was inclined to reduce the vigor of nursing the breast.

The chief difference between this special regimen and the more commonly used and highly successful one, which utilizes complemental feeding of a liquid mixture, is the inclusion of farina in the former for the purpose of converting liquid formulas into semisolid preparations. According to my experience a diet that includes orange juice, cod-liver oil, and complemental feedings of cereal-thickened milk formulas suffices to compensate adequately, throughout a period of three or four months, for deficits in the supply of breast milk, and furthermore, a regimen of this character favors the continuance of maternal nursing. Although the complemental feedings the selected group of fifty-one infants received during the early months of life were not confined to the use of a cereal-milk mixture, it is hoped that the novelty of the liberal diet these young infants received will not obscure the fact that the primary object of this report is to call attention to the possibility of promoting excellent nutrition in infants and simultaneously encouraging maternal nursing by avoiding the use of complemental bottle feedings.

At the conclusion of the first month of life the diet of the selected group of infants included breast milk, farina or oatmeal cooked in milk, cane sugar, and orange juice. Between the ages of 4 and 8 weeks cod-liver oil, sardines in oil, creamed tuna fish, salmon, shrimp, carrots, and canned peas were added to the diet. A white sauce was used to cream the sea fish in order to facilitate the swallowing of foods that otherwise tend to accumulate in the roof of the young infant's mouth. The carrots and peas (skins included) were crushed with a fork but were not strained.

Subsequent periodic additions (Table I) resulted in constructing a very liberal diet for these infants in the first half year of life. This regimen promoted very satisfactory gains in weight (Table II), and its use was accompanied by a continuance of maternal nursing in each instance. This liberal diet did not cause important gastrointestinal disturbances. Occasionally specific food items seemed to be responsible for minor abdominal distress, and in this respect cod-liver oil was on a par with each food that was used. On the whole no reasons were encountered for consistently avoiding or condemning any item listed in Table I.

The satisfactory results obtained with the selected group of fifty-one infants through the use of an exceptionally liberal regimen correspond with those I obtained in Minnesota throughout a period of several

TABLE I

THE SEMISOLID FOODS ADDED TO THE DIET OF INFANTS TO COMPENSATE FOR INADEQUACY OF THE SUPPLY OF BREAST MILK

AGE IN MONTHS	0 TO 1	1	2	3	4	5	6	7
	FOODS ADDED TO DIET EACH MONTH							
	Cow's milk*	Sardines	Asparagus	Egg yolk	Whole egg	Plums	Bacon	Fowl
	Farina, oatmeal	Creamed tuna	Spinach	Custard	Cabbage	Eggplant	Beef, veal	Turnips
	Banana, orange	Salmon, shrimp	Creamed tomatoes	Tapioca	Cauliflower	Cottage cheese	Liver	Rutabaga
		Peas,† carrots	Prunes	String bean	Corn meal	Cream cheese	Vegetable soup	
		Cod-liver oil		Beets	Rice, potato		Celery	
				Applesauce	Jello			
				Pears	Peaches, apricots			

*Cow's milk thickened with cereal.
†Vegetables were crushed but not strained.

TABLE II

AVERAGE BODY WEIGHT OF INFANTS FED A LIBERAL DIET TO COMPENSATE FOR AN INADEQUATE SUPPLY OF BREAST MILK

AGE (MONTHS)	AVERAGE BODY WEIGHT (POUNDS)	
	FEMALES (28)	MALES (23)
Birth	7.2	7.7
1	8.0	8.5
3	11.8	12.7
6	16.7	17.5
9	19.5	20.6
12	21.4	22.8

years, during which time I have consistently tested various modifications of the general scheme of substituting complemental feedings of appropriate semisolid foods for liquid milk mixtures. This program reduced the prescribing of liquid milk formulas to a very low level in my practice. It also increased the incidence and duration of maternal nursing among my patients, and it often enabled me to re-establish breast feeding after it had been discontinued for a few weeks.

In view of the success that attended the promotion of the program that largely eliminated the use of complemental bottle feeding, the feasibility of instituting the same general type of feeding program in the warmer climate of the South has been tested in our outpatient clinics for the past eighteen months. The details of the program devised to compensate for a deficit in the supply of breast milk and also to liberalize the diets of young infants are as follows:

0 TO 1 MONTH

1. Breast feeding every three or four hours, using both breasts each time.

2. Instead of complemental bottle feedings, give cereal cooked either in the milk formula the mother may have started to use or in equal parts of whole cow's milk and water with 5 per cent sugar and a pinch of salt added to the mixture. This cereal-thickened formula is offered by spoon immediately before nursing. The amount given and the frequency with which it is offered are varied in accordance with individual requirements.

3. Add orange juice and cod-liver oil to the diet.

1 MONTH

Add mashed ripe banana and creamed tomato.

2 MONTHS

Add boiled egg yolk, crushed (unstrained) carrots, peas (skins included), apple sauce, prune pulp, prune juice.

3 MONTHS

Add sardines in oil, creamed salmon, tuna fish and shrimp, whole egg, custard, tapioca, potato, cauliflower, asparagus, string beans, vegetable soup.

4 MONTHS

Add ground beef, fowl, beets, cabbage.

The diet now includes breast milk, cow's milk (thickened with cereal), eggs, and a variety of cereals, vegetables, fruits, and meats. Further additions are made

from month to month, but throughout the period the infant's diet is being constructed, a serious attempt is made to avoid bottle feedings of liquid milk mixtures.

The experience we have had with this program in the South indicates that warm climate is no contraindication to its use. The results of testing this special method of feeding in Louisiana and in Minnesota are mutually confirmatory, with respect to the following points:

Cereal-thickened formulas are tolerated well as early as the third day of life; they are a satisfactory substitute for complemental bottle feedings; their use favors the continuance of maternal nursing; they are taken readily by spoon by young infants after a brief period of training; and babies thrive when they are used adequately in conjunction with breast feeding.

The introduction of a wide variety of appropriate, moderately coarse (unstrained), semisolid foods into the diet at an early age seems to be advantageous in several respects. This procedure safeguards nutrition through providing multiple overlapping sources of essential nutrients. It acquaints young infants with the majority of the important flavors and aromas they are apt to encounter during life, and the use of crushed rather than strained vegetables and fruits accustoms them to swallowing moderately coarse particles of food. These accomplishments are of value in that they tend to eliminate the inclination displayed by many babies to gag, to vomit, to refuse food, to acquire aversions to certain foods, and to develop anorexia either when foods with unfamiliar flavors and aromas are introduced tardily into the diet or when a transition from finely strained to coarse, chopped foods is undertaken relatively late. Dr. Eric Clarke, director of the Department of Child Psychiatry at the University of Minnesota, spent several months in my clinic and during this period was particularly impressed with the tendency of good eating habits to persist throughout the period of childhood in patients who became accustomed to a very liberal diet during infancy. His observations agree with my own in strongly suggesting that perhaps the solution of the widespread problem of anorexia in children is contingent to a considerable degree upon establishing good eating habits at an early age by cultivating the infant's acquaintance with a wide variety of appropriate semisolid, moderately coarse, foods.

In conclusion, I recommend the routine use of cereal-thickened milk formulas, fed by spoon to young infants for the purpose of compensating for varying degrees of deficiency in the supply of breast milk. This alternative for complemental bottle feeding has the advantage in that it does not discourage the continuance of maternal nursing.

The introduction of a wide variety of appropriate semisolid foods into the diet at an early age is also recommended. This practice cultivates excellent eating habits which tend to persist. It also safeguards nutrition by providing multiple overlapping sources of essential nutrients.

EMOTIONAL DISTURBANCES OF CONSTANT PATTERN FOLLOWING NONSPECIFIC RESPIRATORY INFECTIONS

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IN TWO other articles[1, 2] a syndrome of anxiety, mild depression with marked compulsive and obsessive manifestations has been described. The onset of these symptoms is invariably associated with upper respiratory infections. Since the diagnostic and early therapeutic problems are primarily of concern to the pediatrician, a summary of these studies may be here in order.

Since December, 1940, twelve children have been observed and treated for diffuse, emotional disturbances following mild upper respiratory infections. In each case a supposedly "normal" child succumbed to an illness variously diagnosed as "flu," "grippe," "tonsillitis," "cold." In each instance the infectious phase was mild, with low febrile response; the duration was short, ranging from a few days to one week. In all these cases a well-defined personality change was established within one month following the onset of the illness.

The analysis of the emotional disturbances revealed a syndrome of anxiety, depression, and anancastic manifestations; that is, compulsive, obsessive, phobic thinking and behavior. Also similar in these cases were the sequences in type and time relationships through which the symptoms developed and resolved themselves: (1) a short interval (one to two days) which was characterized by features similar to a quasi-delirium with motor restlessness, apprehension, tension, and lability in mood; (2) heightened anxieties, depressive mood with an apparent onset of compulsions, and obsessions of varying duration.

Subsequently these children withdrew from their everyday interests. At first the withdrawal was from the less familiar and the more recently acquired expressions of socialization, later from the more superficial interpersonal relationships. Finally, contact with familiar persons was severely disturbed.

At the height of the emotional illness these children were preoccupied, at times "wooden," slightly retarded, sad, at times irritable, uncooperative, demanding, self-accusatory, resentful, fearful, anxious, and terrified. They were busy in the performance of rituals and to them meaningful repetitious acts. Sleep and food intake were frequently disturbed. School work was marked by failure.

Recovery was slow but also revealed certain patterns of progression. The first indications of change were usually an improvement in mood

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and motor activity. Regressions which followed were of varying duration. These regressive interests and activities, appropriate for chronological levels lower by several years than patients' actual age, seemed marked in proportion to the severity of the entire emotional illness. A gradual subsidence of the gross compulsive and obsessive activities came relatively late in the recovery phase. In all cases, one of the last adjustments was the ability to cope with the school program fulfilling both the academic and social requirements. It would seem that the recovery phase reversed the process of withdrawal. The children felt increasingly secure enough to return to interests in enlarging fields of activity. Their interpersonal readjustments started in the family group and later extended to multiple contacts with various people.

To illustrate this syndrome the observed similarities of symptoms and chronology have been stressed. Contents of thought, the expressions of such phenomena as "depression" and "anxiety" and "anancasms" were as individual as the child itself (for summary of clinical data see Table I).

Within nine months after the onset of the illness these children were considered "well." However, it was only through a therapeutic approach and when recovery was well under way that a more accurate evaluation of the total personality could be made. These so-called "normal" children showed potentiality and capacity for pathologic emotional manifestations. In the relative security of their everyday life these children were able to offset their personality liabilities by personality assets. For as yet not clearly understood reasons, the very occurrence of illness here, as elsewhere, seemed to have served as the trigger stimulus to the appearance of gross emotional disturbances.*

The etiologic factor or factors were obscure. Studies to ascertain the presence of a specific bacteriologic agent or to evaluate vitamin deficiencies were noncontributory. This syndrome was not associated with drug intoxications. Only two children obtained sulfathiazole in appropriate dosage after the emotional disturbances had become manifest. The other children were offered supportive measures during the infectious phase, and three were treated with small doses of phenobarbital for "nervousness." With the exception of one child,† these patients were free from chronic illness or long-term disabling condition.

A survey of the possible pertinent literature did not reveal descriptions of this type of symptomatic neurosis in association with mild upper respiratory infections.

In differential diagnosis were considered sequelae to so-called "influenza," psychotic states associated with epidemic influenza, emotional disturbances associated with chronic encephalitis, some forms of deliria, anxiety states, conditions allied to manic-depressive psychosis, and the

*The description of this illness is identical with that presented in references 1 and 2.
†This child had congenital heart disease with mitral stenosis.

more classical "compulsive neurosis." Although certain similarities could be seen with the behavior observed in the present series and in any one of the above-mentioned clinical entities, not one offered the initiating upper respiratory infection followed by quasi delirium which ushered in the compulsive behavior of varying duration.

The other illnesses may befall individuals of differing personality structures, whereas here the prepsychopathologic personality make-up was characteristic, well-defined, and similar in all of the twelve children.

Children who succumbed to these disturbances were invariably subservient, docile, cowed by authority, perfectionistic in their strivings, and meticulous in personal habits. They were nonaggressive and repressed. Because of these features these children were held in high esteem by parents and teachers. Their childhood associates were usually critical and belittled the nonaggressive qualities. I believe that the personality structure of these children is of greatest importance in understanding the course and psychologic expressions of the illness here described. These children have potential capacity for psychopathologic manifestations. When physical sickness strikes, these children with pent-up emotions of hatred and associated guilt will put all their old means of coping with emotional difficulties into full play. The realization that these usually effective methods, even in grossly exaggerated forms, are no longer sufficient to suppress the inherent feelings and thoughts is most disturbing to the patient. It is of interest to note that every child interpreted his illness as "punishment" for some ill-understood wrong committed by him. (For further personality and environmental statistics, see Table II.)

Children with the milder forms of this illness may be treated on an ambulatory basis by a pediatrician. With recognition of the syndrome, he can introduce appropriate supportive measures. Assurance can be given to the parents that the symptoms are not synonymous with "insanity." A favorable prognosis may be offered with spontaneous recovery to be expected in about six months—not later than nine months. With some understanding of the "psychologic mechanisms" involved, the pediatrician will be able to assist parents to an attitude of tolerance toward this illness and may guide patient and parents to more satisfactory interpersonal relationships than those obtained prior to the onset of illness.

The children with the more severe forms of this illness can be adequately cared for on the pediatric service of a general hospital. Hospitalization during the early quasi delirium and anxiety states is advised. The intensive psychotherapy which is definitely indicated for this group should be undertaken only by especially trained psychiatrists. The supportive measures include treatment of the upper respiratory infection. A diet with high vitamin content offered in frequent small feedings seems best tolerated by these children. Fluids ad lib. are

TABLE I

	CASE 1	CASE 2	CASE 3	CASE 4
Initials	B. K.	P. M.	R. C.	E. B.
Age and sex	10 yr., M	14 yr., M	10 yr., F	8 yr., M
Date of onset	Nov. 11, 1940	Second week of Dec., 1940	First week of Jan., 1941	Jan. 12, 1941
Temperature	101 to 102° F.	101° F.	?	101° F.
Initial symptoms and complaints	Sore throat	"Cold"; vomiting; headache	"Cold"; nausea; headache with "burning of eyes"	"Severe sore throat"
Duration of upper respiratory infection	One week	"Few days"	One week	Three days
Interval between physical illness and emotional disturbance	One week	Two weeks	Immediate	One day
Complaints and symptoms	Fear of choking; fear of illness; distraction — staring; rituals about eating, washing, urination, praying; indecisions; motor retardation; sexual fantasies; withdrawal; inability to concentrate; failure in school work	Fear of illness; staring into space; rituals about and preoccupation with stair walking, religion, salaaming; irritability; retardation; distraction; withdrawal; failure in school work	Fear of illness; hand wringing; head scratching; preoccupation with sexual themes; irritable—uncooperative; very fussy and meticulous; demanding reassurance; withdrawal; failure in school work	Restless; subjective feeling of confusion; ritualistic behavior at night—amnesia for this type of behavior; preoccupation with religion and sexual themes; retarded; withdrawn; failure in school work

Mood	Depressed—labile	Depressed—labile	Depressed, anxious, tense	Depressed and anxious, labile
Sleep	Fair; at times restless, dreams	Good	Difficulty in going asleep; terrifying dreams	Restless, interrupted; night terrors
Food intake and weight change	Fair, very slow eating; (?) weight loss	Fair; (?) weight loss	Fair; (?) weight loss	Poor; (?) weight loss
Personality	High average intelligence; slow, quiet, timid, reserved; sensitive, conscientious; obedient, nonaggressive; friendly, wistful; generous, loyal; religious; anxious	Average to high average intelligence; active, outgoing; "fussy," meticulous; religious; tense, anxious; usually cheerful and pleasant	Average to high average intelligence; shy, inquisitive, affectionate; obedient, fussy, "model child in school"; usually cheerful; concerned about illness; suggestible	Average intelligence; active, alert; inquisitive, obedient; affectionate; very responsible; usually cheerful
Course of illness	Nov., 1940-Jan., 1941, increasing emotional difficulties; hospitalized Jan. 23, N. H. H.; discharged Feb. 12; gradual improvement; clinic visits three times weekly until April, 1941; considered "well" June, 1941	Clinic visits every week; gradual improvement in mood; obsessive and compulsive manifestations dropped out in March, 1941; difficulty in school work and lack of interest in play until May, 1941; gradual return to usual activities in June, 1941	Gradual steady improvement in three and one-half months; "well" by mid-April, 1941	Four weeks out of school; general improvement through February and March; complained of inability to concentrate in April; improvement in school May; "well" by June, 1941

TABLE I—CONT'D

	CASE 5	CASE 6	CASE 7	CASE 8
Initials	M. G.	J. D.	H. B.	J. T.
Age and sex	14 yr., F	12 yr., F	8 yr., F	5 yr., F
Date of onset	Second week of Jan., 1941	Third week of July, 1941, at summer camp	First week of Aug., 1941, at summer camp	Last week of Jan., 1942
Temperature	?	101°	101-102° F.	101-102° F.
Initial symptoms and complaints	Headache; sore throat	"Laryngitis"; sore throat	Sore throat; "bad cold"	Cold; "flu"; vomited
Duration of upper respiratory infection	One week	One week to ten days	"About one week"	One week
Interval between physical illness and emotional disturbance	Three weeks	Second day of illness	Third day of illness	Second day of illness
Complaints and symptoms	Fear of illness—brain tumor (?); irritable—fussy; obsessively clean and tidy; rumination about self; retarded; withdrawn; failing in school work	Fear of death by choking; fear of being alone; fear of burglars; fear of "cat man"; irritability, distractability; fussy, demanding behavior; night terrors; had to return home from summer camp	Scared "something terrible would happen"; choking sensations; refusal to be alone, insisted on seeing mother; irritable, uncooperative, labile; fussy about cleanliness, frequent changes of dresses; night terrors with fear of being pursued and apprehended by a strange male figure; thought she could not see well; had to return home; withdrawn, distractable	Refusal to leave mother; feeling of impending doom; irritable, fussy, demanding; had to have several baths a day; repeated change of clothing; "cleaned house constantly"

Mood	Depressed, crying	Slightly depressed, apprehensive	Labile, apprehensive	Apprehensive, slightly depressed
Sleep	Poor, restless	Very poor, difficulty falling asleep; wants somebody in room to talk to her, wakened by frightening dreams	Poor—unwilling to sleep alone in room; frequent wakening by terrifying dreams	Poor, refused to sleep alone; night terrors, pursued by large cats, about to be apprehended by animals
Food intake and weight change	Poor—weight loss, 5 pounds	Poor, fussy eater; weight loss, (?) 5 pounds	Fussy--food must be served "just so"; no apparent weight loss	Loss of appetite; food had to be served "just so"; all dishes had to be "clean"; no apparent weight loss
Personality	Average to high average intelligence; self-conscious; sensitive, devoted to mother; efficient, conscientious, careful, inclined to be fussy; usually cheerful	Superior intelligence; active; very conventional; sensitive, conscientious, wistful, meticulous; tense; jealous of younger sister	Good intelligence; active; easily persuaded; conscientious, obedient, sensitive; much concerned about illness in members of family; interested but frightened by current events; neat and orderly of possessions; vied with older sister for parents' affection	Good intelligence; affected manners; considered very good, docile, obedient; anxious about 16-year-old brother; easily frightened, cautious; very neat and clean
Course of illness	Gradual improvement in mood and motor activity; obsessions became less; active in house; did not return to school for rest of academic year; considered "well" by June, 1941	Improvement gradual; sleep and appetite normal in six months; fears receded slowly; aggression against sibling marked until May, 1942; considered well June, 1942	Poor school performance in fall, with preference to stay at home; gradual decrease of symptoms; improved by Feb., 1942, when parents took child to Florida	Gradual improvement; returned to Sunday school in six weeks; refused to go to kindergarten during spring; gradually would leave house; obsessive symptoms disappeared by early summer, 1942

TABLE I—CONT'D

	CASE 9	CASE 10	CASE 11	CASE 12
Initials	R. S.	P. P.	F. S.	S. B.
Age and sex	9 yr., 6 mo., M	9 yr., M	10 yr., M	11 yr., M
Date of onset	First week of April, 1942	May 7, 1942, mild U.R.I.; cervical glands swollen	Aug. 31; admitted to N.H.H., Sept. 2, 1942; discharged Sept. 5, 1942	Sept. 28, 1942
Temperature	Temperature not taken	May 13, "very sore throat"; temp., 100° F. during U.R.I.; 104.5° F. with sore throat	103° F. on admission	101° F.
Initial symptoms and complaints	"Mild cold"	As above	Headache, dizziness, vomiting; hospital diagnosis: pneumococcal fever, congenital heart disease; pneumococcus in N. and T. culture	"Slight cold"
Duration of upper respiratory infection	Three to four days	Five days (from time of onset of "sore throat")	Six days	Three days
Interval between physical illness and emotional disturbance	Third day of illness	Fifth day	Seventh day after onset of illness	Second day of illness
Complaints and symptoms	Second day of illness choking sensation; very apprehensive; two days later started touching furniture, pictures, books, pillows and trees with buttocks and then would kiss part of object touched by buttocks; irritable, uncooperative; seemed preoccupied, withdrawn; afraid to play with "rough boys" on street; refused to go to Hebrew school	Choking sensation first day of sore throat; writing in air with index finger; compulsive circular motions with fingers; tapping of feet, humming; fear of G-men; would shoot brother in fantasy; threatened to kill brother and sister; alternating marked restlessness with deep sleep; state of consciousness *not* clouded; very dependent on parents	Scared father (now in jail) would climb through window and kill him with gun; very apprehensive about burglars concealed in house; constant rumination about wrongs done by father; refused to let mother go to work—very dependent on her; constantly cleaning and scrubbing floors in compulsive manner; fussy, irritable; withdrawn, refused to go to school	Scared something would happen—thought walls of room would fall in on him; jumped out of second-story window to avoid disaster; thought repeatedly he would have to fly away and was moving arms in flying motion; preoccupied with theme of levitation; excited, irritable, "wound up"; dependent on mother

Mood	Surly, slightly depressed	Apprehension very marked; tearful, labile	Apprehensive, labile, slightly depressed	Very apprehensive, slightly depressed
Sleep	Poor, restless, wakened frequently by "bad dreams"	Restless sleep—jabbering about aggressive acts	Poor—frequent wakening with terrifying dreams; afraid to go to bed	Sleep restless
Food intake and weight change	Prior to present illness, voracious eater; ate less but food intake still good	Appetite poor; refused much food but at times would grab food and stuff it into mouth with fingers; (?) weight loss	Loss of appetite; very choosy about what to eat	Loss of appetite
Personality	Dull normal intelligence; obedient, nonaggressive; "mama's boy"; cautious, fairly neat; feelings easily hurt; school performance never very good but worse since illness; participated very little in school activities	Good intelligence; "perfect boy"—obedient, affectionate, nonaggressive; enuretic, nail-biter; very conscientious, worrisome; very religious; overmeticulous with school work	Average intelligence; very responsible (is father to his younger brother and sister); conscientious, obedient, sensitive; made excellent adjustment to restrictions because of cong. heart disease—glad he does not have to fight; religious; fairly neat and orderly; had adjusted well to father's absence from home	Superior intelligence; serious, very cautious, obedient; very sensitive about relatively short stature, afraid of getting hurt; not very aggressive—plays much by himself; interest in aeroplanes for two years; meticulous; conformer to social conventions; affectionate
Course of illness	Course unknown; mother uncooperative	Became increasingly aggressive and active; obsessive symptoms disappeared gradually during summer, 1942; entirely well by Sept., 1942; able to resume school work	Gradual clearing of all symptoms in two months; resumed all former activities	Improvement marked in six weeks; able to resume all activities

TABLE II

Socioeconomic status		
Proletarian background		3
Lower to middle-class background		6
Upper middle-class background		3
Racial descent		
Old American stock		3
Italian		2
Irish		3
German		1
French-English-Irish		1
Russian-Jewish		2
Religious affiliations		
Protestant		5
Catholic		3
Catholic-Protestant		2
Jewish		2
History of obvious psychoses or mental disease in families (None)		
6 families	1 parent "nervous," irritable	
1 family	1 parent (mother) of very low intelligence	
1 family	Both parents anancastic, tense, father treated for alcoholism	
1 family	Mother diabetic and hypochondriacal	
1 family	Father subject to depressive moods and gastrointestinal symptoms	
1 family	Father in jail for theft	
General physical condition of patients prior to illness		
Has been good to excellent, except E. B. who had mumps with hallucinations during the acute stage (4 years of age), and F. S., who had congenital heart disease with mitral insufficiency.		
Intelligence		
Superior	2	
High average	1	
Average	8	
Dull normal	1	
Behavior		
No overt behavior problems prior to illness		

essential. For the more disturbed child, bed rest is indicated for about one week. During this phase sedation with appropriate doses of phenobarbital twice a day is helpful. For the very restless child small doses of paraldehyde in oil, administered per rectum, and given at night are effective. It is important to give the child restful sleep. Continuous tubs at 96° for from forty-five to sixty minutes as tolerated once or twice a day are efficacious aids to sedation. Physical restraint is not advised. The children gain comfort from the presence of an attendant in the room during the most disturbed phase. Such constant supervision also serves as the best precaution against suicidal attempts, self-mutilation, and escape. In the present series no suicidal attempts were noted. Precaution, however, is indicated as the individual may turn his aggressions against himself. Glasses, knives, pins, and strings should be removed from the room. After the most disturbed phase has passed, the children should be transferred to the ward. Contact with other children

is beneficial and gives the patient assurance that his peculiar behavior is not punished by isolation. When sleep and food intake have returned to normal, the mood has become stable, and patient shows some interest and ability to cope with his environment, discharge from the hospital may be considered.

Contact with the psychiatrist during the acute phase of the illness is very desirable. Psychotherapy can be started on the ward and later continued on an ambulatory basis. In these twelve children the therapeutic problem was focused on the theme of aggression and hostility, helping the patient to become fully aware of these feelings and to help him channel these into appropriate, socially acceptable expressions.

Prognosis for this illness is good. With supportive therapy the acute phase passes within two to three weeks; the residual anancastic behavior subsides, in about six to nine months. There is a spontaneous recovery; however, those children who work out their problems under psychotherapeutic guidance will show a more stable personality adjustment after the illness than that obtained prior to the emotional disturbance.

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THE USE OF THE SUPPOSITORY AS A VEHICLE IN SULFONAMIDE THERAPY

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THE various sulfonamides are usually administered in plain or enteric-coated tablet form by mouth. Enteric-coated tablets are designed to prevent gastric irritability and to facilitate intestinal absorption, inasmuch as they are unchanged in the stomach. Unfortunately, however, they frequently pass unaltered through the intestinal tract. The sodium-sulfa combinations are prepared in ampoules for intravenous use, but must be employed with caution. They may also be used in proper solution by hypodermoclysis with comparative safety.

It is well known that the giving of sulfonamides by mouth is frequently attended by nausea or vomiting, thereby interfering with the absorption of the drug and the desired fluid and food intake. It is important that those distressing symptoms be obviated, especially in the treatment of infants and young children in whom acidosis and dehydration are so prone to occur during the course of illness. Toward that end, when gastric disturbances have appeared during the oral administration of sulfonamides, it has been my practice, for at least two years, to prescribe such drugs in suppository form per rectum. The base employed in making the suppository is cocoa butter, which melts quickly in the rectum, leaving the drug available for reasonably rapid absorption. Any desired dosage may be utilized. However, 7.7 gr. and 15.4 gr. suppositories of the preferred sulfa drug have been found satisfactory in most instances. The rectal dose is twice that given by mouth.

Thirty minutes before instituting treatment, a cleansing warm water enema should be given. The parent or nurse is then instructed to insert one suppository into the rectum, for retention, at stated intervals. The buttocks should be held firmly together for fifteen to twenty minutes or strapped with adhesive plaster if necessary to prevent expulsion of the medicament.

Gastric irritability due to oral administration of sulfonamide has been avoided entirely through the use of the sulfonamide in a suppository base, per rectum. Blood level estimations have demonstrated that this method of treatment is as efficacious as that by mouth.

3720 FANNIN STREET

TRICHINOSIS DURING CHILDHOOD

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ALTHOUGH there have been numerous reports of epidemics of trichinosis throughout various parts of the country, there have been very few reports of the occurrence of this disease in children. Individuals of all ages are susceptible to the trichinae, but, of course, children under 3 or 4 years of age rarely eat foods that might contain the parasite. This paper is based upon a study of eighteen cases of trichinosis that occurred in children between the ages of 2 and 15 years during the interval of November, 1941, to February, 1943. During the same interval a total of approximately sixty patients with trichinosis were observed in the Windber Hospital among patients of all age groups. Most of these cases occurred during the months from October to December, 1941, at which time there was a small epidemic of the disease.

Trichinosis or trichiniasis is an acute febrile illness caused by the *Trichinella spiralis*. The parasite was first observed by Richard Owen in 1835 and was first called *Trichina spiralis;* the name was later changed to *Trichinella spiralis*. Leidy found trichinellae in pork in the year 1847. Until recent years this disease was considered to be relatively rare. However, during the past several years the incidence of trichinosis has been found to be much higher than was previously considered. At the National Institute of Health a total of 4,893 diaphragms were examined from persons who died in the hospitals in thirty-fiye states and the District of Columbia; in addition to this, 5,531 examinations were made in other laboratories, making a total of 10,424 examinations up to August, 1940. It was found that 1,547, or 14.8 per cent, of the diaphragms that were examined were positive for the parasite. It therefore becomes quite evident that approximately 15 per cent of the general population has been infected with the trichinae.

Season and sex do not have any great influence in the incidence of the disease, and age is a factor only because young children under the age of 3 or 4 years do not ordinarily eat foods which might contain trichinae. (However, our series includes one patient 2 years of age and another patient 3 years of age.) We have seen more patients during the late autumn and early winter months than at any other time of the year; this is probably due to the greater popularity of foods such as country sausage at such times of the year. One attack of trichinosis does not confer a permanent immunity, and cases have been reported in patients in whom two or more attacks have occurred.

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Drake, Hawkes, and Warren,[1] in 1935, summarized the various epidemics in this country that had been recorded. These are as follows: 50 cases with four deaths in Boston in 1892; 14 cases in New York State in 1916; 43 cases in Albany in 1929; 14 cases in East St. Louis in 1930; 29 cases in Pennsylvania in 1931; 43 cases in Atlantic City in 1933; and a small epidemic resulting from jerked bear meat in 1932. Drake and co-workers reported an epidemic of 51 cases in Maine in 1935.

McNaught and Anderson[2] examined 225 diaphragms from consecutive autopsied cadavers in five hospitals in San Francisco and found an average of 24 per cent trichinous diaphragms. Marble, Skoog, and Bucholz[7] reported an epidemic of thirteen cases among soldiers at Camp Edwards, Mass., in 1942.

LIFE HISTORY OF TRICHINELLA

When an individual eats trichinous meat, the larvae are freed from their cysts by the digestive juices of the stomach. The larvae then penetrate into the intestinal mucosa. Here the male and female sexual forms develop and mate anywhere from forty to seventy-two hours after the meat is eaten. The females then give birth to living young within six to seven days after infection, and larval production may continue for six or more weeks. The newborn trichinae measure about 100 μ in length and 6 μ in width. They enter the intestinal lymphatics from about five to seven days after the primary infection and are disseminated throughout the body through the blood stream. They are carried to all parts of the body but have a particular predilection for the voluntary muscle where they are found about the sixth or eighth day after ingestion and where they eventually become encapsulated. Although the larvae are found chiefly in the voluntary muscle, they may also affect almost any organ of the body, including the respiratory system, nervous system, kidneys, liver, and skin.

SYMPTOMS

In the typical acute case of trichinosis, there are certain unmistakable symptoms. The usual course of events in an adult is as follows: initial gastrointestinal symptoms occurring about two to eight days after eating the infected meat (this consists of abdominal pain, nausea and vomiting, and attacks of diarrhea); a few days after the gastrointestinal symptoms appear, the patient develops severe headache, chills, fever, and edema of the eyelids. The puffiness of the eyelids is one of the most constant symptoms of trichinosis, and Kaufmann[3] states that he has observed this symptom in from 60 to 80 per cent of the patients whom he had seen over a period of five years. However, in most of our cases that occurred during childhood, we did not find such typical symptoms. The symptoms in general in most of the patients consisted of fever, headache, gastrointestinal upsets, muscular pains, and oc-

casionally edema of the eyelids or edema of the extremities. As a rule, the symptoms were very similar to those of an ordinary attack of grippe, and in many instances the diagnosis had to be made on the basis of laboratory findings or a history of ingestion of infected meat or a history of other cases in the family.

SUMMARY OF EIGHTEEN CASES

Age.—The ages varied from 2 to 15 years, including one patient 2 years and one 3 years of age. There were five cases at the age of 8 years.

Sex.—The sexes were equally divided, there being nine females and nine males.

Season.—Seven of the eighteen patients were admitted between the latter part of October, 1941, and the early part of December, 1941. There were no cases between the months of March, 1942, and October, 1942.

Symptoms:

Fever: Fever was a constant symptom. Every patient had an elevated temperature, the temperature varying from 100 to 104° F. The average temperature on admission was 102° F.

Chills: Three patients had chills. These were all in the older group of children.

Headache: Twelve of the eighteen patients complained of severe headache.

Gastrointestinal Symptoms: Gastrointestinal symptoms were quite frequent. Nausea and vomiting were present in six patients. Diffuse abdominal pain was present in eight patients and in two instances there was pain in the right lower quadrant of the abdomen simulating appendicitis.

Edema: In contradistinction to adults, edema was not a common occurrence in this series of patients. Edema of the face was present in four patients. Swelling of the lower extremities was present in two patients, simulating acute rheumatic fever. Edema was of a transient nature and would disappear at the end of one or two days.

Muscular Pain: Muscular pain was a common symptom, being present in ten patients. The location of the pain would vary; in some instances there was severe chest pain; other patients had severe pain in the lumbar muscles; in a few instances there was pain in the lower extremities, particularly the knees and ankles.

Laboratory Findings.—Although eosinophilia has always occupied an important place in the diagnosis of trichinosis, we were surprised to find a relatively low instance of eosinophilia in cases of trichinosis during childhood. Some of the patients showed no eosinophilia whatsoever, although the diagnosis was eventually proved on the basis of the history of ingestion of infected pork and on the basis of a positive precipitin test. The highest eosinophile count was 32 per cent whereas in adults eosinophile counts of as high as 80 per cent were encountered.

It is important to note that eosinophilia is only transient. In the patient with an acute case of trichinosis it does not appear until at least one week after the infection has occurred and will often subside within another week. In one instance in which the diagnosis was proved by biopsy, the eosinophile count was as follows: Nov. 5, 1941, eight days after having eaten trichinous pork, the eosinophile count was 32 per cent. Three days later (November 8) there were only 12 per cent eosinophiles, and on November 15 the eosinophile count returned to a normal of 4 per cent. It is misleading to rely on eosinophilia for the diagnosis of trichinosis, because the blood count may be taken too early or too late in the course of the disease.

Total White Blood Counts: The total white blood counts varied from 7,050 to 36,900.

Sedimentation Rate: The sedimentation rate was slightly to moderately increased.

Intradermal Tests: An intradermal test has been developed during the past few years which has become of considerable value in the diagnosis of trichinosis. The antigen employed for this test is prepared from powdered trichinae larvae. The test consists of injecting 0.01 c.c. of 1:10,000 dilution of the antigen intradermally. The test is usually read in from fifteen to twenty minutes after the injection of the antigen. A positive test consists of a wheal surrounded by a zone of erythema. In some instances a delayed reaction appears at the end of thirty-six hours. It is therefore essential to observe the patient at the end of this time. The skin test does not become positive until the end of the second week following infection. Skin tests were performed in ten of our patients, with positive reactions in eight.

Precipitin Test: The National Institute of Health has developed a precipitin test for the diagnosis of trichinosis. This test was performed in all of our patients with positive results in sixteen. There were two negative precipitin tests in instances of definite trichinosis. It is important to note that the precipitin test does not become positive until about ten days after the initial infection. McNaught, Beard, and Myers[5] state that 97.2 per cent of their patients with active trichinosis eventually gave positive intradermal reactions and that there was a great correlation between the intradermal and precipitin reactions. There were several false positive precipitin reactions. Such reactions occurred particularly in one patient with typhoid fever and in another patient whose condition eventually proved to be undulant fever. It is important, therefore, to correlate the history, the clinical picture of the case, and the precipitin test and not rely exclusively on the precipitin test for diagnosis. Persistently negative immunologic reactions are of more value in ruling out trichinosis than are positive ones in establishing the diagnosis. Initial negative tests in patients who later showed positive reactions are of important significance.

Biopsy: More conclusive evidence of trichinosis is the finding of the larvae in a muscle biopsy. Obviously it is not practical to make biopsies on all patients because of the objection of parents to having this procedure performed. We were able to obtain only two biopsies, both of which were positive.

Electrocardiogram: In view of the fact that the *Trichinella spiralis* is disseminated throughout the body, we felt it would be interesting to make electrocardiographic tracings on some of the patients. No electrocardiographic abnormalities were found in eight patients on whom tracings were taken. Other observers have reported various electrocardiographic changes in adults, including inversion of the T wave in Lead II, low amplitude of the QRS wave, occasional evidence of intraventricular block, and temporary prolongation of the P-R interval.

CLINICAL COURSE OF THE DISEASE

Most of the patients had a relatively mild illness. They were usually symptom free approximately one week following admission to the hospital. One patient was quite ill for a period of three weeks, during which time he had severe joint pains and developed a marked anemia. There were no permanent complications. Follow-up study revealed no residual muscular pains. There were no recurrences.

DIFFERENTIAL DIAGNOSIS

Trichinosis may simulate many diseases. It must be differentiated from the following:

1. Acute nephritis. The facial edema, edema of the ankles, and fever often simulate the symptoms seen in acute nephritis.
2. Acute gastroenteritis. Gastrointestinal symptoms simulate those seen in gastroenteritis.
3. Acute appendicitis may be suspected and an unnecessary operation may be performed.
4. Influenza.
5. Sinusitis. Severe headache often simulates that seen in sinusitis. It is interesting to note that the conditions of several of the adult patients had been diagnosed as sinusitis for several days before trichinosis was really suspected.
6. Angioneurotic edema.
7. Typhoid fever.
8. Rheumatic fever.
9. Undulant fever.
10. Pleurodynia.
11. Pneumonia. The fever and chest pains which are often seen frequently lead one to suspect early pneumonia.

The most frequent incorrect diagnoses are grippe and influenza, acute nephritis, acute sinusitis, and acute rheumatic fever. Undoubtedly many cases of trichinosis have been diagnosed as la grippe.

PROGNOSIS

The prognosis of trichinosis depends on several factors:

1. The number of trichinae in the affected meat and the amount of meat eaten.

2. General health and resistance of the host.

3. Localization of larvae.

Kaufman states that a severe diarrhea with resulting dehydration may be a large contributing factor to a fatal outcome. The presence of larvae in the brain is of great significance, and encephalitis is a fairly common complication of trichinosis. In our series of patients, there were no fatalities and no recurrences, nor were there any residual symptoms.

TREATMENT

There is no specific treatment for trichinosis. Chemotherapy is of no value in the treatment of this disease. Various chemotherapeutic agents have been tried including silver arsphenamine, antimony, potassium tartrate, sulfanilamide, and sulfathiazole. None of these agents seems to have any beneficial effects on the disease, although silver arsphenamine enjoyed a considerable degree of popularity some years ago. Symptomatic treatment consists of the use of sodium salicylate or aspirin plus an opiate if necessary for relief of pain. Fluids should be forced. In some instances it is necessary to administer fluids intravenously because of the severe vomiting and diarrhea.

CASE REPORTS

The following are typical cases:

CASE 1.—F. C., white female, 3 years of age. On October 29 the patient ate some fried pork. On November 2 she developed edema of the eyelids. The left eye was almost completely closed. She was very feverish and had severe backache; also, a mild cough for two or three days; no vomiting or diarrhea. She was admitted to the hospital Nov. 5, 1941. The temperature on admission was 100° F. Examination showed marked edema of both cheeks. There was some puffiness of the eyelids.

Urinalysis was negative. On November 5 the blood count was as follows:

Red blood cells	3,880,000	Neutrophiles	28
White blood cells	16,050	Small lymphocytes	38
Hemoglobin	68%	Large lymphocytes	2
		Eosinophiles	32
			100%

November 8—white blood cells, 15,650, with an eosinophilia of 12 per cent. Skin test with trichinella antigen was positive. On the day following admission the facial edema subsided, and on the following day the patient was symptom free. She was discharged Nov. 11, 1941. Biopsy of the gastrocnemius muscle showed the presence of encysted larvae of *Trichinella spiralis*. A precipitin test performed by the National Institute of Health November 23 was positive in dilutions of 1:80 to 1:1280.

CASE 2.—J. D., white female, 6 years of age. This patient was admitted Dec. 1, 1941, with chief complaints of severe frontal headache and fever. For three or four days preceding admission she was very feverish and had a severe frontal headache. The temperature was 102° F. on admission and eventually rose to 104° F.

Blood count was as follows:

Red blood cells	4,080,000	Polymorphonuclears	78
White blood cells	8,200	Small lymphocytes	15
Hemoglobin	75%	Large lymphocytes	2
		Mononuclears	5
			100%

Undulant fever agglutination test was negative; Widal test was negative. X-ray examination of the sinuses and chest was negative. We were unable to account for this patient's symptoms and made a careful inquiry as to the possibility of her having eaten infected pork. We discovered that about one week before admission she had eaten some country sausage that was not thoroughly cooked. A blood precipitin test performed by the National Institute of Health December 5 showed a positive reaction in dilutions of 1:80 to 1:1280. This patient had a temperature of from 102 to 104+ F. for six days before admission. After admission it subsided, and she was discharged December 9, 1941, free of any symptoms.

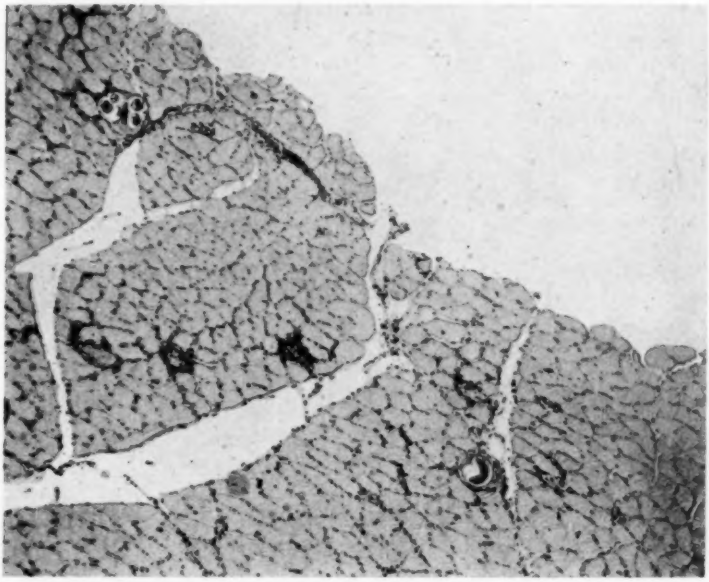

Fig. 1.—Biopsy of gastrocnemius from the patient in Case 1. Encysted larvae and round cell infiltration are shown.

CASE 3.—M. F., white female, 15 years of age. This patient came to the hospital March 15, 1943, with complaints of facial swelling and severe headache. The initial impression that she gave was that of acute nephritis. Urinalysis was negative. Blood count on day of admission showed 10,000 white blood cells with

no eosinophiles. The facial edema persisted, and March 16 there was an eosinophile count of 10 per cent. On March 22 the eosinophile count was 28 per cent. The intradermal skin test and blood precipitin test March 27 were both negative. This patient gave a history of having eaten country sausage and questionably cooked pork two weeks before admission. Although this patient had a definite case of trichinosis, both the skin test and precipitin test were negative. This is undoubtedly due to the fact that both of these tests were performed approximately one week following her initial symptoms and had not, as yet, had an opportunity of becoming positive.

SUMMARY

1. Eighteen cases of trichinosis during childhood are reported.

2. Trichinosis is not uncommon during childhood.

3. It may simulate many other diseases, particularly nephritis, sinusitis, la grippe, and acute gastroenteritis.

4. Eosinophilia may not be present during the early stages of the disease and during the late stages of convalescence. Eosinophilia cannot always be relied upon in making a diagnosis.

5. The intradermal test and precipitin tests are of great value in corroborating a diagnosis of trichinosis.

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THE TREATMENT OF KAPOSI'S VARICELLIFORM ERUPTION WITH SULFONAMIDE DRUGS

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SINCE Kaposi's description of the disease now known as Kaposi's varicelliform eruption, only twenty-five cases were reported in the literature up to 1936. Since that date, nineteen additional cases have been described in English literature.

Opinions vary as to the etiology of the disease, but all observers agree that the clinical manifestations are characterized by fever and pustular umbilicated lesions superimposed on a previously existing atopic eczema. The seriousness of the disease is reflected by McLachlan and Gillespie's[1] report of five deaths in sixteen cases and Graves and Dowman's two cases,[2] both fatal.

We were able to find only one report of the disease, in which sulfonamides were used for treatment. A woman, age 72, who had eczema, bronchopneumonia, and Kaposi's varicelliform eruption, was treated with sulfanilamide in the dosage of 80 gr. daily for three days. The pustules were singularly resistant to treatment, and the patient died.[3]

Recently we have treated three patients with Kaposi's varicelliform eruption with sulfonamides, and the prompt response in two of these will be noted by the following case reports.

CASE 1.—S. M. A., 8 months of age, weight, 17½ pounds, with a known case of atopic eczema, developed a scratch under his right ear on June 19, 1941. This area became swollen and red and was accompanied by enlargement of the regional lymph nodes. On June 21 a vesicular eruption appeared at the involved area and the infant became feverish (102° F., axillary). By June 23, the time of admission to the hospital, the rash had spread widely over the scalp, face, and neck. *Staphylococcus aureus* was cultured from the lesions. The temperature reached a peak of 105° F. rectally on June 24. On the evening of this same date sulfanilamide, 5 gr. every four hours, was started, being reduced to 2 gr. every six hours on June 28 and discontinued on June 30. Following the administration of sulfonamide the fever fell by lysis, the temperature becoming normal in forty-eight hours and, except for a slight rise four hours later, remained normal thereafter. Healing of the umbilicated vesicular lesions occurred synchronously with the reduction in fever and by June 30 was practically completed.

CASE 2.—R. G. S., 4 months of age, weight, 13 pounds, 13 ounces, was admitted to the hospital March 8, 1942, with a history of eczema of the face since the age of 2 weeks. On March 1, 1941, the infant was attacked by an acute intestinal upset and on March 8, by an exacerbation of the eczema. Upon admission to the hospital the infant was found to have a temperature of 104° F., an erythematous rash covering the lower half of the face, and an umbilicated vesicular eruption involving the forehead, cheeks, neck, upper anterior chest, and wrists. Vomiting, diarrhea, and a temperature of 104° F. developed. Sulfanilamide, 2 gr. every six hours, was begun, and a transfusion was given. Five days later, the medication was

changed to sulfadiazine, 3¾ gr. every six hours. At this time the temperature was still 103° F. and new skin lesions were still appearing. A blood culture was negative. Fourteen days after admission, the fever abated and the skin gradually cleared.

CASE 3.—R. C., 14 months of age, weight, 19 pounds, was admitted June 5, 1942, from another hospital where he had been treated for eczema. Two days before admission the baby became irritable, refused to eat, and typical umbilicated pustules appeared over face, arms, and upper chest. The temperature rose to 105° F. On the day of admission, sulfathiazole, 3¾ gr. every four hours, was started. Two days later the dose was given every six hours, and this was continued for three days. Within forty-eight hours the temperature dropped to normal, and within a week the varicelliform disappeared completely.

None of our patients had previously been vaccinated against smallpox, and none of them had been exposed to a recently vaccinated person. Even if this disease should prove to be caused by a virus, there seems to be at least a complicating infection of some importance which responds favorably to sulfonamide drugs. No secondary infections developed among the other patients in our wards or among the nursing staff.

CONCLUSIONS

1. Kaposi's varicelliform eruption is a serious complication of atopic eczema.

2. In two of three of our patients, sulfonamides brought about a prompt and spectacular recovery.

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OBSTRUCTION OF THE LARGE BOWEL IN NEWBORN INFANTS DUE TO CONGENITAL BANDS

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WITHIN a six-month period at the Jewish Hospital in Philadelphia there have been two unusual cases of intestinal obstruction in newborn infants. Numerous authors have reported cases in which there was obstruction of the duodenum or other parts of the small bowel due to congenital extrinsic bands, incomplete bowel rotation, or congenital atresia and stenosis. There have also been infrequent cases of obstruction of the colon. However, the latter, except for a single case reported by Glover and Hamann,[11] were due to atresia or stenosis, or were associated with obstructions in the small intestine. In Glover's case a band around the splenic flexure of the colon was found at operation. The patient died, but no autopsy was performed. The authors prefer to believe that an incomplete bowel rotation was present at the same time. It appears then that no proved cases of obstruction of the colon in newborn infants due to extrinsic bands in the absence of other bowel malformations are present in the literature surveyed. The clinical picture of small bowel obstruction in the neonatal period is well known and has been fully reviewed in other works. It is the purpose of this paper to describe the picture found when there is a simple large bowel obstruction.

In adults high obstruction produces early vomiting and little abdominal distention; low obstruction produces abdominal distention, and vomiting is late in appearing, if present at all. In infants similar clinical pictures are found. Ladd and others have adequately demonstrated the picture existing in high obstructions, the condition more commonly encountered and written about. Low obstruction in infants produces a symptom complex akin to that found in adults with lesions obstructing the colon, as shown by the following two cases.

CASE 1.—Baby W., a white male weighing 5 pounds, 13 ounces, was delivered on July 7, 1942. The infant passed two normal meconium stools on July 8 and July 9. On July 10 it was noted that he nursed poorly and regurgitated small amounts of his feedings. Beginning on that day he passed one normal stool daily for three days, after which there were no more bowel movements. On July 13 the abdomen was described as being distended. Peristalsis was audible. Hypodermoclysis of normal saline with 2.5 per cent dextrose solution was started. On July 15 peristalsis was no longer heard. The child then began to vomit, the vomitus consisting of most of his food mixed with bile. A leucocyte count done the same day showed 5,000 leucocytes per cubic millimeter, with a differential count of 42 per cent neutrophiles and 58 per cent lymphocytes. The patient continued on a downhill course, expiring on July 16, 1942. At the time of death the child weighed 5 pounds, 8 ounces, a total

From the Newborn Nursery of the Jewish Hospital, Philadelphia, Pa.

weight loss since birth of only five ounces. The clinical diagnosis was "intestinal obstruction with paralytic ileus, etiology undetermined."

In summary, the following points are emphasized: (1) Distention was noted six days after birth and was progressive; (2) vomiting was a minor symptom and did not become severe until after the distention was marked; (3) stools were passed until just before death; (4) there was little weight loss.

A post-mortem examination was done eight hours after death. The interesting findings were limited to the abdomen. There was a moderate amount of brownish-tinged, slightly cloudy fluid in the abdomen. The serosa of the bowel and the parietal peritoneum were covered with a yellowish brown exudate which was easily removed. The abdominal digestive tract showed distended loops of bowel which were intensely injected. At the hepatic flexure of the colon there were numerous congenital bands extending down from the undersurface of the liver, causing the ascending colon and the proximal portion of the transverse colon to lie in apposition. From this point to the rectum the bowel contained no fecal material and the mucosa was normal. The entire remaining portion of large and small bowel showed marked injection of the mucosa and patchy areas of thinning of the bowel wall with a loss of normal mucosal pattern. There were no gross perforations. There was a large amount of fecal material from the middle of the jejunum to the ascending colon. There were no congenital strictures in any portion of the gastrointestinal tract. There was no evidence of faulty or incomplete rotation of the intestinal tract. Except for patchy areas of atelectasis in the lungs, all the other organs appeared normal. Microscopy confirmed the gross findings as reported. The final diagnosis was "intestinal obstruction at the hepatic flexure of the colon due to congenital bands; secondary early peritonitis."

CASE 2.—Baby L., a white male weighing 7 pounds, 13 ounces, was delivered on Jan. 22, 1943, the abdomen being reported as slightly distended. The child had a normal meconium stool on January 23. The following day the abdomen became more distended. The rectal temperature was 99.8° F. Although the child was not vomiting, gavage feedings were started, and sulfadiazine, gr. 1 every three hours, was given to combat a suspected hidden infection. On January 26 there were five small, formed meconium stools. It was noted that the abdomen, although distended, was soft. No report as to the nature of peristalsis was made. The temperature gradually rose and reached 104° F. on January 27. There was no vomiting at any time. Three normal stools were passed daily. Hypodermoclysis of saline solution was started. An x-ray taken the same day was interpreted as follows: "There is a large amount of air in the large and small intestines. This is suggestive of a congenital anomaly, possibly a partial small intestinal stenosis." On January 30 the child had a single bloody stool. A statement was entered on the chart at this time: "intestinal obstruction is apparently not present." On February 1 the child expired. There was no excessive weight loss. The clinical diagnosis was "congenital malformation of the gastrointestinal tract (functional or organic)."

In summary, the following points are emphasized: (1) Distention appeared early and was progressive; (2) vomiting was present only on the day of death; (3) stools were passed until two days before demise; (4) there was little weight loss.

A post-mortem examination was done five hours after death. The interesting findings were limited to the abdomen. The abdominal cavity contained some bloody serous fluid. The cecum, ascending colon, and entire small bowel were distended. There were numerous bands extending from the undersurface of the liver to the hepatic flexure of the colon. At this point the lumen of the bowel was almost completely occluded. The bowel immediately proximal was gangrenous, and the mucosa was ulcerated. The small bowel was distended with feces and gas. Distal to the obstruction the colon was collapsed and clean. The serosa was smooth throughout. There were no other congenital anomalies. The final diagnosis was "intestinal

obstruction at the hepatic flexure of the colon due to congenital bands leading from the undersurface of the liver to the colon; necrosis of proximal large bowel."

DISCUSSION

The cause of the obstruction in both infants was a peritoneal sheet extending from the undersurface of the liver to the hepatic flexure of the colon. In both instances the overlying band constricted the bowel lumen enough to produce a gradual accumulation of material proximal to the obstruction, although some fecal material was able to pass. Since vomiting was not a prominent symptom, sufficient food was ingested to reach the obstructed area. This eventually led to pressure necrosis of the proximal bowel, and in one infant, to a secondary peritonitis. In neither instance was the true nature of the condition suspected. Although the amount of distention was out of proportion to the amount of vomiting, a large intestinal obstruction was not considered. Whitaker[7] has demonstrated in adult cadavers a high incidence of congenital bands leading from the undersurface of the liver to the colon. Although in his cases there was no obstruction, there is no reason why some of these might not constrict the bowel and produce symptoms early in life, as in the two cases presented.

Abdominal distention out of proportion to the amount of vomiting, in spite of repeated bowel movements, should suggest to the physician the presence of an obstructing band around the large bowel in newborn infants.

It is hoped that in the future the condition will be recognized early. The surgical procedure in early cases is obviously simple (cutting bands). If intervention is decided upon too late, more radical operations will be necessary.

SUMMARY

1. Two unusual cases of large bowel obstruction in newborn infants due to congenital bands extending from the undersurface of the liver to the hepatic flexure of the colon are presented

2. The similarity of the symptom complex to that found in adults with lesions obstructing the colon is discussed.

3. The early recognition of the possibility of such bands producing intestinal obstruction is emphasized.

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TYPHOID FEVER IN A SEVEN-MONTH-OLD INFANT

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TYPHOID fever in an infant 7 months of age is of sufficient interest to warrant reporting not only because of the rarity of the disease in infancy but also because of the difficulties which may be encountered in making a correct diagnosis.

A survey of the literature reveals that the youngest case of acquired typhoid fever was reported by Weech and Chen[1] in an infant 21 days old in China. In 1902 Griffith and Ostheimer[2] collected together 139 cases of typhoid fever occurring in the first year of life, 110 of which they considered as definitely typhoid, 46 probably typhoid, and 17 doubtful typhoid. Tupas and Quintos[3] stated that in the German Children's Hospital at Prague, where typhoid fever is endemic, among 1,530 typhoid patients only 10 (0.6 per cent) were 1 year of age or less. These authors also reported that of 223 patients admitted with typhoid fever in the Philippine General Hospital, none was under 2 years of age.

According to Holt,[4] in 14,000 patients admitted to the Babies' Hospital, New York, in a period of thirteen years, there were but five patients with typhoid fever in the first year of life, the youngest being 8 months old. Holt,[5] in his latest textbook, states that among 252 typhoid cases in children at the Harriet Lane Home only four were infants under 1 year of age, the youngest being 4 months. Reports by Abt and Abt,[6] Blackader,[7] Griffith,[8] Morse,[9] and Adams[10] also indicate the rarity of typhoid fever in the first year of life.

CASE REPORT

L. H., a white male infant, was born Feb. 8, 1942. He became ill with fever and vomiting on Sept. 15, 1942. On September 30 the fever reached 105° F. rectally, and vomiting became worse so the child was admitted to a local hospital in the country. In the hospital he was unable to retain any food. He also had a mild diarrhea of four to five loose stools daily which varied in color from normal to dark green.

On October 1 the patient developed a generalized maculopapular rash which was diagnosed as measles, and he was immediately referred to the Charity Hospital. By this time the child had become stuporous.

Past History.—At birth the child weighed 6½ pounds. He was weaned when 4 days of age and was placed on an evaporated milk formula. In 1940, two years previous to the birth of her child, the mother contracted typhoid fever and was treated in the Charity Hospital. She was discharged as cured. The past health of the child had been good until the present illness.

Shortly before the onset of this illness, the patient was given unboiled well water while visiting in the country. According to the history, two other cases of typhoid fever occurred in individuals drinking water from the same well.

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Physical Examination.—On admission to Charity Hospital, the child weighed 17 pounds, 10 ounces, and his total length was 70 cm. He was dehydrated and stuporous, and his fever was 105° F. The skin was dry and hot, and large areas of erythema were present on the flexor surfaces of the arm. Pink, irregular, maculopapular eruptions were present on the trunk, arms, and face.

Inspection of the mucous membranes of the mouth failed to reveal Koplik's spots. There was no conjunctivitis. The lips were dry, cracked, and bleeding. The pharynx was normal. The respirations were shallow and occurred at the rate of 58 per minute. There was slight dilatation of the alae nasae and an expiratory grunt. The lungs were clear on auscultation and normal on percussion. The abdomen was distended and tympanitic but no tenderness was found. The abdominal organs could not be adequately palpated due to the distention.

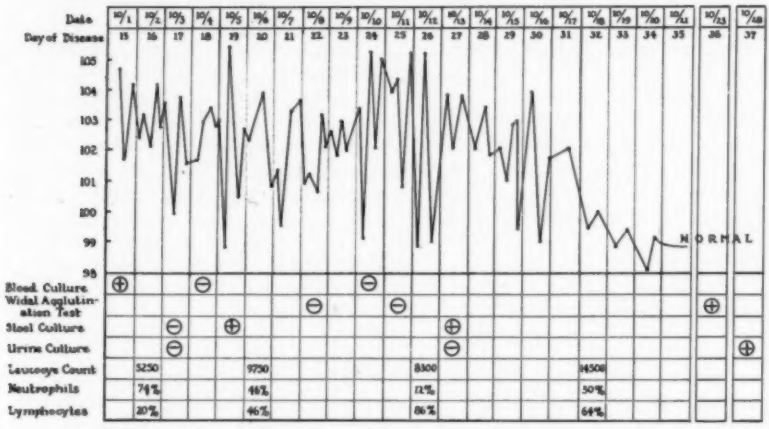

Fig. 1.—Temperature curve and laboratory data of a case of typhoid fever in a 7-month-old infant (Case 1).

Clinical Course.—Because of the fever, rapid respirations, and cough, a provisional diagnosis of pneumonia was made in spite of our inability to confirm this diagnosis on physical examination. A diagnosis of acidosis was also made on the basis of rapid respiration and a history of diarrhea, but no chemical study of the blood was done to confirm this.

On admission the patient was given 100 c.c. of one-sixth molar sodium lactate intravenously and 250 c.c. of 5 per cent glucose in Ringer's solution by hypodermoclysis. One thousand cubic centimeters of 5 per cent glucose in distilled water was then started in a continuous intravenous drip during the next twenty-four hours. Because we suspected pneumonia, 15 gr. of sodium sulfadiazine were given intravenously followed by a similar dose every twelve hours for two doses. The drug was then administered orally every four hours until it was discontinued on October 5.

Since x-ray of the chest was negative the diagnosis was next focused on some form of sepsis. Blood cultures were taken on the day of admission. A spinal puncture ruled out meningitis. The spleen was palpable on October 3. Stool and urine cultures were ordered.

By this time a diagnosis of typhoid fever was seriously considered, particularly since the blood study showed a leucocyte count of 5,000 with 74 per cent polymorphonuclear leucocytes. The patient was isolated immediately.

Following intravenous and subcutaneous administration of fluids, dehydration disappeared, stupor subsided, and the patient appeared much stronger. Respiration became deeper and much more forceful. A high caloric liquid diet and fluids were administered by stomach tube. The blood cultures taken on October 1 were reported positive for *Eberthella typhi* on October 5. Sulfadiazine was discontinued at this time. A blood transfusion of 50 c.c. of whole blood was given on October 5 and repeated on October 11 and 13. Enemas and rectal tubes were used to combat distention. The roseola disappeared in three days, but the temperature elevation continued remittently, ranging from 100 to 104° F., as shown in Fig. 1. A Mantoux test using 0.1 c.c. of a 1:1,000 dilution of old tuberculin was negative.

The patient improved progressively and by October 10 took his formula voluntarily. He began to gain weight, and although still continuing to have fever, he appeared happy and alert. The temperature gradually subsided to normal on October 19, approximately thirty-three days after its appearance.

Laboratory Findings.—The Kline and Kolmer tests were negative. Urine cultures were positive for *E. typhi* only once, October 28. Stool cultures were positive consistently up to October 28, after which they were consistently negative. As previously mentioned. the blood culture taken on October 1 was positive, but susequent blood cultures taken on various occasions were negative. Agglutination tests for typhoid, paratyphoid, dysentery, tularemia, and undulant fever were consistently negative up to October 23. The Widal agglutination tests were positive 1:80 on October 23, 1:160 on October 28, and 1:640 on November 14. Agglutination test run on the mother's blood were negative for typhoid on two occasions. Her stool and duodenal drainage cultures were also negative.

During convalescence the child ate well and gained weight so that at the time of discharge, November 24, he weighed exactly 22 pounds.

COMMENT

Practically all authors who have reviewed the subject have emphasized the difficulty of making the diagnosis of typhoid fever during infancy. The symptoms are often misleading. Our patient presented a typical history and findings of typhoid fever. It is well known that typhoid fever in infancy often is ushered in with remittent fever and vomiting. Diarrhea may not be encountered. In fact, a patient with typhoid often suffers from constipation. Stupor may also be present in typhoid fever but is much more commonly encountered in meningitis.

Bronchitis is often associated with typhoid fever. Roseola is easy to see and recognize only if one has typhoid in mind. Otherwise, it may often be confused with other exanthemas, such as measles, which happened in our case. The absence of conjunctivitis and Koplik's spots should exclude rubeola. Fever, enlarged spleen, roseola, and diarrhea cannot help but point to a diagnosis of typhoid fever.

It is stated that typhoid fever in infancy carries a high mortality. This may have been true in former years but at the present time if the disease is recognized early and fluid and nutrition adequately maintained, the mortality should be no higher during infancy than in any other period during childhood. However, the United States Census Bureau[11] figures show that the typhoid death rate per 100,000 in 1940 in infants under 1 year of age was 9 per cent (actually four deaths),

as contrasted to a death rate of from 2.5 to 5.7 per cent in the other age groups.

As to the geographic incidence of typhoid fever in this country, it is well known that the number of cases occurring in the southern states is much higher than in the northern states. The incidence in Louisiana is among the highest in the United States.[11]

We are certain that the source of infection in this child was the infected well water. It seems interesting that the mother had also contracted the disease two years previously and had apparently recovered completely from the disease.

This case teaches us that typhoid fever may occur during infancy unless public health measures are instituted to protect the water and food supply. There is no immunity against the disease during early infancy. Most authors believe that the low incidence of typhoid during early childhood can be attributed to less exposure. It is interesting to note that the Widal agglutination titer in our patient did not rise until the fever had subsided, approximately five weeks after the onset of the disease. Moreover, the mother who had contracted typhoid fever two years previously had a negative agglutination titer.

SUMMARY

A case of typhoid fever with recovery in an infant 7 months of age is reported.

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PROBLEMS IN SAFEGUARDING ADOPTIONS

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ALTHOUGH there is no way by which we can determine with accuracy the exact number of children adopted in a single year, the widespread popularity of this subject in the magazines, newspapers, on the screen, and over the radio has made us think of it as "big business" in the United States today. The U. S. Children's Bureau estimated on the basis of actual figures from nine selected states in 1936 that at least 16,000 children were adopted in the United States in a single year. As these selected states did not include New York, Illinois, Pennsylvania, or Ohio where it is known that many adoptions occur, the true figure is probably even higher than this estimate.

Since many of the 16,000 persons adopted are children unable to speak in their own behalf, their welfare deserves careful attention, for by adoption the whole life plan of a child may be altered. Early adoption laws did not recognize the social aspects of this procedure, and it was more than half a century after the passage of the first statutory provision for adoption in the United States that social safeguards made their appearance in the legislation of individual states. Even yet a number of states still operate under nineteenth century adoption laws. It is not unusual in these states to find the judge of a local court unaware of important social implications when he makes a decision by which the natural parents as well as the child are divested of all legal rights and obligations each to the other and all the rights, privileges, and responsibilities of own parents are transferred to the parents by adoption.

PLACEMENT OF THE CHILD

The first step in an adoption proceeding and a very important one is the selection of a home for the child where his potentialities will be recognized and he is likely to find emotional satisfaction. This does not mean "any good home" will do, but, instead, a home must be found which is suited to the needs of the child. Sometimes a child born into a family is a misfit there, despite the fact that he is the result of two blended personalities. Two objective, thoughtful, understanding parents will probably be able to work out the problems presented in such a situation, but when an unrelated child is placed in a permanent home the relationships are even more difficult, and real professional skill is necessary in order to make sure the persons selected to become his future parents by adoption are those with whom he is most likely to be

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happy and emotionally well adjusted. These persons must be willing to accept him wholeheartedly and be able to provide for him the environment best suited for his future development.

It is easy to find a home for a child, for the number of persons wanting children far exceeds the number of children available for placement, but skill is necessary in selecting the right home for each child.

Ordinarily cautious foster parents will not wish to consider a plan for adoption with all this means in terms of permanence, inheritance rights, and responsibilities until the child has lived with them for a long enough time to give them the assurance that it is this particular child they wish to make a member of their family and not just any child. The outcome of hasty adoptions may be unfortunate for both the child and the adopting parents.

In order that the foster parents may have the assurance that the child taken into their home will not be removed unnecessarily, the safest procedure is to act through an agency that has authority to accept guardianship of the child and to plan for him in place of the parent. Under such conditions it is unnecessary for the adopting parents to have any personal contact with the natural parents, and when the time for final adoption arrives, it is the agency from which consent must be obtained rather than the natural parents.

It is understandable that persons desiring a child for adoption wish to have a young child so that they can maintain the illusion that the child is really their own. However, there are many "unknowns" in a foster child that are less likely to be found in a child born to the parents. It is important, therefore, to delay placement plans until the child is old enough so that his particular needs can be determined and the selection of a home and parents made for him with these needs in mind. A child placed for adoption is not only placed for the period of his babyhood but for life. In the opinion of the U. S. Children's Bureau, placement should be delayed until the child is at least 4 months old. Under such conditions the potentialities of the child may be evaluated before the plan for his future is determined.

The age of the child in relation to the ages of the foster parents should also be carefully considered. One child-placing agency has accepted the policy that the life expectancy of the foster parents shall be such that the child may reach maturity during their lifetime. It is also important that the adopting parents be young enough to share the interests of the child.

One benefit to the child frequently not recognized when considering the advantages of placement by an agency is the continuing interest maintained by the agency. When the plans for a child's placement are made by an individual who is without professional skill, it is doubtful whether he will follow through to see that the child's interests have been safeguarded and that the adoption plan really materializes. All too

often children are discovered who for years have been members of a foster family and yet have not been accorded the protection legal adoption carries with it. Possibly it is not until the inheritance rights of the child are questioned that the harm done to the child is discovered.

ADOPTION SAFEGUARDS

The need for safeguarding adoption practices extends even beyond the safeguards found in the adoption laws. It is important, therefore, also to have legislation that will limit child placing to agencies with a competent and qualified staff so as to make certain the professional skill is provided that placement for adoption demands. It is likewise important that all related laws in a state, such as the juvenile court laws, laws relating to guardianship, laws pertaining to termination of parental rights, and the vital statistics laws, be carefully considered so that the adoption law may be properly correlated with them. It is for this reason a uniform adoption law, such as has frequently been suggested, is not likely to serve the purpose, since it would be extremely difficult to draft a law that would be in conformity with the related laws in every state.

A satisfactory adoption law, important as it may be, is not sufficient in itself, for unless an intelligent and adequately supported plan is developed for the administration of the legal provisions, these may have little meaning.

It has been interesting to note the steadily increasing interest in protective adoption legislation in the individual states. These laws provide protection not only for the child who is to be adopted, but also for his parents and the adopting parents. Even without a uniform law, considerable uniformity has been achieved by the growing acceptance of certain desirable safeguards which include the following:

1. *A Social Study or Investigation Following Every Petition to Adopt a Child.*—This is particularly important when no previous study has been made of the adoption situation. For the child placed by a qualified agency it is probably safe to assume that a careful study has been made of the adoptive home prior to the decision to place the child there. Knowledge of the child's adjustment to the home has probably also been obtained by the placing agency during the months following placement when the agency has continued to supervise the child in the home. But unfortunately, many adoptive placements are made independent of agencies and without any inquiry about either the child or the prospective foster family. The desire of a family for a child is not in itself sufficient evidence that it should be permitted to adopt a particular child or perhaps even any child. Only when all the facts are known about a petition for adoption can we be certain that the proposed adoption is wise and will promote the best interests of the child involved.

On Sept. 1, 1942, the laws of thirty states and the District of Columbia required a social study of each petition for adoption. In four additional states and Hawaii it was left to the discretion of the court to decide whether or not this study was desirable.

The advantage of centralizing in the state department of public welfare the responsibility for making arrangements for the social study has been recognized in nineteen states. This procedure assures greater uniformity in practice and makes it possible for the state department to give leadership in the administration of the entire adoption program together with its interrelated aspects.

The laws of eleven states have made it the responsibility of the court to make or arrange for the social study. In five of these states the state department of public welfare is included as one of the resources that may be utilized for making the social study, and in South Dakota the report must be approved by the state department; in two other states a licensed child welfare agency or the county department of welfare must be used, but in the four remaining states a probation officer or an individual appointed by the court may be asked to accept the responsibility for this specialized task. Since few of these persons have the professional training essential for making the necessary study, many pertinent points may be overlooked entirely in the information obtained.

2. *A Report to the Court After the Social Study.*—The social study loses much of its value unless the information obtained is presented to the court in such form that it will provide a basis for the final decision, which, of course, rests with the judge hearing the adoption. In all but one state having provision for a social study, provision has also been made for a formal report to the court. In seventeen states the report must include a recommendation, and in three additional states the making of a recommendation is implied, but in ten states only a report of the findings is necessary. In three states the content of the report is not specified, and in one state the court itself is responsible for the investigation.

Even though a report without a recommendation may clearly indicate the desirable or undesirable features of the adoption, added clarity is provided when the report contains a definite statement recommending the action that seems desirable and for the best interests of the child with the reasons for such a recommendation. In an adoption proceeding the future happiness of a child and the adopting family is under advisement. It is therefore important for the decision to be made according to the individual situation rather than in conformity with rigid rules which may be satisfactory in principal but which do not apply in the particular situation under consideration.

3. *A Required Residence Period for the Child in the Home Before the Adoption Becomes Final.*—Child-placing agencies have for years been aware of the importance of a residence period for the child in the foster

home—a "period of absorption" this has been called—when the child and the foster parents have an opportunity to become adjusted to each other. Child-placing agencies are able to control the plans for their own wards, but children placed without the benefit of agency services frequently have been adopted before there was any assurance that the adjustment between the child and the foster parents would be satisfactory. Indeed, adoptions were sometimes consummated when the child had never been in the foster home or had been there only a few days.

In order that children placed independently of child-placing agencies and the foster families with whom these children are placed may have the same protection as children placed by agencies, a period of residence in the home before the legal responsibilities conferred through adoption are assumed is required in the adoption laws of twenty-nine states and the District of Columbia. In the early laws the residence period required was usually six months. Unfortunately, in several states the court was given permission to waive the requirements at its discretion when it was satisfied that the proposed home and the child were suited to each other. In the more recent laws the tendency has been to increase the residence period to one year, and the court is without authority to waive the requirement. The residence period is being accepted as a period for supervision of the child in the foster home. The laws of some states have specifically provided for this supervision by means of an interlocutory decree with a supplementary report at the close of the interlocutory period. In other states without provision for an interlocutory decree, provisions have been made so that the child in the home will have the benefit of careful supervision before the adoption is completed.

Supervision with service and assistance to the prospective adoptive parents has great value in protecting the welfare of the child. However, since the need for supervision is a question for social determination, there are certain advantages in giving discretion to the supervisory agency rather than to the court for the decision as to the need for continued supervision.

4. *A Carefully Drawn Consent Provision That Respects the Rights of the Natural Parent.*—When parental rights have been terminated either by court action or through voluntary relinquishment, guardianship rights should be transferred to the placing agency authorized to act in place of the parents and to give the required consent.

Many adoption laws, especially early ones that followed nineteenth century tradition, authorized the court hearing the adoption petition to decide on the fitness of a parent to give or withhold consent to the adoption. The tendency in the newer adoption laws is to remove this authority from the court hearing the adoption proceedings and make it the responsibility of the court hearing children's cases. Actually two issues are involved and separate hearings are therefore essential:

(1) a determination of the fitness of the parent to retain his rights with relation to the child and (2) a determination of the merits of the proposed adoption in so far as the welfare of the child is concerned.

Consent from a legally qualified authority should be required in every adoption. If the parents have retained guardianship rights their consent should be obtained. When this is not possible because one or both parents have disappeared or are thought to be incompetent, a hearing in the court hearing children's cases with notice to the parents should be held. After presentation of all the facts, the court can then make its decision about termination of parental rights on the basis of the evidence and without being confused by a pending adoption. Following termination of parental rights, it is important to provide a substitute with authority to act in place of the parent in the matter of consent.

Although all questions involving court action for the removal of a child from his parents should be definitely settled before the adoption is heard, a method should also be provided by which the parent who wishes voluntarily to be released from his parental obligations may relinquish his rights after a careful inquiry has been made of all the circumstances and consideration of the best interests of the child.

When such a safeguard has been provided, it is improbable that a petition to adopt will be granted unless consent to the adoption has been obtained.

5. *A Plan for the Protection of All Official Adoption Records From Persons Who Have No Legitimate Reason to Be Permitted Access to Them.*—Early adoption records were considered public records like those of other court actions. Beginning in 1917, however, there has been a steadily growing appreciation of the need for protecting these records from the eyes of curiosity seekers and sometimes from "scandalmongers" as well. Now twenty-five states and the District of Columbia provide this protection, and in three additional states limited protection is provided.

Even when legal recognition was taken of the need for protecting records of adoption, the first laws providing for this limited access to "parties in interest," except upon order of the court. When later it was found the interpretation of this term differed widely and determination of a "party in interest" was ordinarily left to the discretion of the clerk of the court or a deputy in his office, a remedy was provided in some states and access to the adoption records was limited to "parties to the action." This means only persons with the right of access are those persons or agency representatives whose names appear in the record because they have given consent or have otherwise been a party to the proceeding. Before accepting a child for adoption, therefore, prospective foster parents should make certain that parental rights have been terminated and guardianship transferred to an agency. Otherwise the

consent of the mother or the natural parents may be necessary at the time of legal adoption and the parents thereby become "parties to the record" with a right to see the adoption record.

6. *Restrict Jurisdiction in Adoption to Residents of the State and, Except in Exceptional Circumstances, to Residents of the County Where the Adoption Petition Is Filed.*—There are obvious advantages in limiting the filing of petitions for adoptions to residents of the county or at least to residents of the state. This is particularly true when a social study is required and information must be obtained about the adopting parents.

The lack of protection for adoption records has probably influenced some prospective adoptive parents to file adoption petitions in jurisdictions other than the one in which they reside. With the progress that has been made in safeguarding the records and removal of the fear that information about the child will become a subject of general knowledge in the community where the foster parents live, the desire to have the adoption heard outside the community will be lessened materially. At the present time, the laws of twenty-four states, Alaska, and the District of Columbia limit adoption jurisdiction to residents of the state and/or to residents of the local jurisdiction in which the petition is filed. In five states, Alaska, and the District of Columbia only residents of the state may file petitions for adoption, but in nineteen additional states the petition must be filed in the county or town where the petitioners are resident. In ten of these nineteen states the petitioners must also be residents of the state.

7. *A Plan for a Report of Every Adoption to the Division of Vital Statistics in Which Proof of Birth Is Included Together With the Date of the Adoption and Sufficient Information About the Foster Parents to Make Possible the Filing of an Adoption Certificate in the New Name of the Child and in the Names of the Foster Parents.*—A provision requiring the filing of official reports of every adoption would make possible an accurate statistical count of the number of adoptions in each state as well as some additional information about the children adopted and the persons adopting them. Only eighteen states require that a report of each adoption be sent to the division of vital statistics, and even in these states the information contained in these reports is not uniform. Therefore, complete knowledge about adoptions granted in the United States can be obtained only by compiling figures from individual counties. In many counties, because no statistical record is kept of adoptions granted, it is practically impossible to obtain figures on a national scale.

A number of states has made provisions either in the vital statistics law or the adoption law so as to permit the birth certificate of an adopted child to be changed and the child's legal name to appear on any documents presented in verification of his birth and citizenship. However,

there has been little uniformity in the procedure followed. Some states have prepared a special certificate in the child's legal name which certifies the sex of the child, the date and place of his birth, the registration number of the original birth certificate and the date it was filed. Other states prepare a new certificate of birth but change the names so that it appears that the child was actually born to the adopting parents.

Confusion has arisen because some states issue special certificates only for children born in the state, whereas others will issue these only for children adopted within the state. As a result a person born in one state and adopted in another may be unable to obtain a certificate of birth in his name by adoption and is thereby deprived of the protection to which he should be entitled.

The present demand for proof of age and citizenship have brought forcibly to the attention of state and federal authorities the importance of a uniform procedure that will satisfy the need of the person or agency demanding these and will also protect the individual from having the circumstances of his birth made known. This has been accomplished in the few states using a certification of birth as described above for all persons desiring proof of birth. When such procedure is followed, the document presented to prove birth and citizenship does not indicate either adoption or birth out of wedlock and the individual to whom it is issued is spared any possible embarrassment because of the circumstances of his birth.

Although significant progress has been made by making available to an adopted child an official record in his legal name which will show his new family relationship and the basic facts about the date and place of his birth, complete protection for adopted children will not be achieved until the restrictive provisions in many of the existing laws are removed and authority is given to provide reports of adoption in the department of vital statistics in those states now without such provisions.

CONCLUSION

Legislative safeguards in adoption are important, but it is equally important that all legislation be strengthened by administrative practices so the intent of the laws may be actually realized. Too many laws —good ones, too,—have never really served the purposes for which they were intended because no satisfactory provision was made for their administration. The very best adoption law will be of little avail if it is not accompanied by an intelligent, adequately supported administrative plan.

The well-informed physician has an excellent opportunity to interpret the need for the observance of such legal and administrative safeguards as are available in his state and may stimulate interest in the establishment of additional safeguards when adequate protection has not been supplied for children who are subjects of adoption petitions.

PULMONARY MANIFESTATIONS FOLLOWING INGESTION OF KEROSENE

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ACCIDENTAL ingestion of kerosene among young children occurs more frequently than is generally recognized. Roentgenologic examination of such patients observed at Grady Hospital during the past two years has drawn our attention to the fact that pulmonary manifestations are very frequently encountered.

The effect of kerosene on the human organism has been studied in a number of papers. Bliss,[1] in 1898, described the death of an 18-month-old infant following the ingestion of 2 oz. of kerosene. LeGludie and Turlais,[2] in 1914, conducted experimental studies to determine the toxicity of kerosene. Their autopsy findings on rabbits which were given lethal quantities of kerosene per stomach tube revealed pulmonary congestion and hemorrhage. Other opinions concerning the effect of kerosene following its ingestion vary widely. A case is quoted in which one man suffered no ill effect after the ingestion of 750 c.c. of this substance.

Waring,[3] in 1933, conducted clinical and experimental studies concerning the pulmonary manifestations following kerosene ingestion. From his experiments on dogs he concluded that it was aspiration and not absorption from the gastrointestinal tract that produced the death of the animal. Nunn and Martin,[4] in 1934, reported a study of seventy-four cases of kerosene and gasoline poisoning and arrived at similar conclusions. However, the opinions regarding the effect of kerosene do not seem to be unanimous. In *Holt's Diseases of Infancy and Childhood*[5] the following statement is made: "It (kerosene) is rapidly absorbed and excreted through the lungs, where it appears to cause local irritation and diffuse pneumonia."

The following study is devoted to the pulmonary manifestations associated with kerosene poisoning and is subdivided into three parts. The first part is a clinical study of thirty-three patients, with a roentgenologic study of twenty-two of these patients observed during the past two years. In the second part an autopsy is described of an 18-month-old child who died approximately five hours after ingestion of about 150 c.c. of kerosene. The third part consists of an experimental study to determine the pathogenesis of pulmonary lesions in animals. An attempt will be made to correlate the observations made in these studies.

From the Departments of Pediatrics and Roentgenology, Grady Hospital and Emory University.

CLINICAL STUDY

Thirty-three patients with kerosene poisoning were admitted during the last two years. The patients ranged from 1 to 3 years of age. The amount of kerosene ingested was at times unknown but usually ranged from one swallow to one-half a glass. The patients were examined in the hospital at intervals ranging from thirty minutes to forty-eight hours after kerosene intake.

In the thirty-three patients reviewed, fever ranging from 99 to 104.5° F. was observed in thirty. Patients with average uncomplicated cases had a fever of three days' duration. Vomiting of nonprojectile type occurred in sixteen patients. Some of these vomited several times. The vomiting was noted almost immediately after ingestion but did not persist longer than a few hours. Coughing was noted in thirteen patients and appeared immediately after ingestion. Ten patients were drowsy on admission to the hospital, and two patients were in a comatose condition. Clinical signs of pneumonia were present in eight patients. The criteria for these findings were fever in the presence of diminished or tubular breath sounds, diminished resonance or percussion, and râles. The mere presence of râles was not considered sufficient evidence for the diagnosis of pneumonic consolidation. It will be seen that there is a remarkable difference in the number of cases which showed clinical evidence of pneumonia and those which revealed roentgenologic evidence of consolidation. Leucocytosis was present in sixteen patients. Urinalysis revealed no constant abnormal findings.

CLINICAL COURSE

There were no fatalities in this group. Two of the patients developed fluid in addition to consolidation. In one patient the fluid disappeared spontaneously, and no chest tap was necessary. The second patient developed empyema which required surgical drainage. With the exception of these two patients with complications, symptoms and signs abated within from two to five days.

The usual clinical course in kerosene pneumonia is illustrated by the following summaries:

CASE 1.—M. R., a 17-month-old colored female, ingested five swallows of kerosene four hours prior to admission. She was given magnesium sulfate at home and vomitted twice before entering the hospital. Examination revealed a temperature of 101° F. but no drowsiness. On examination of the chest fine râles were found posteriorly at both lung bases. A chest film on admission showed numerous confluent mottled densities throughout the left lower lung field, and the bronchovascular markings at the right costophrenic angle were accentuated (Fig. 1). After three days there was slight clearing of the densities throughout the left lower lung field. The right lower lung field revealed several mottled densities (Fig. 2). Further follow-up studies revealed residual consolidation in both cardiophrenic angles. The leucocyte count on admission was 11,000, with an essentially normal differential count. On supportive therapy the child made clinically an uneventful recovery in seven days.

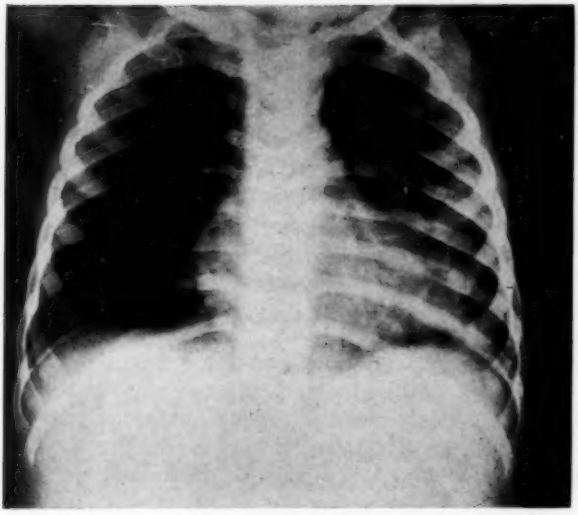

Fig. 1 (Case 1).—Roentgenogram four hours after ingestion of kerosene. Coarse mottled densities in the left lower lung field; accentuation of lung markings in right cardiophrenic angle.

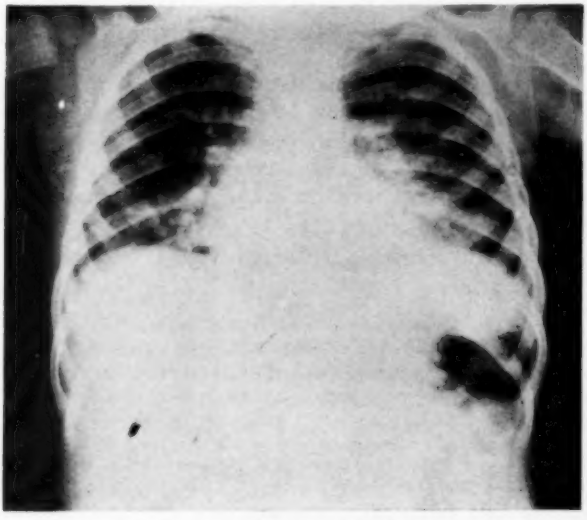

Fig. 2 (Case 1).—After three days. Slight resolution of consolidation in left lower lung field; mottled densities in right lower lung field.

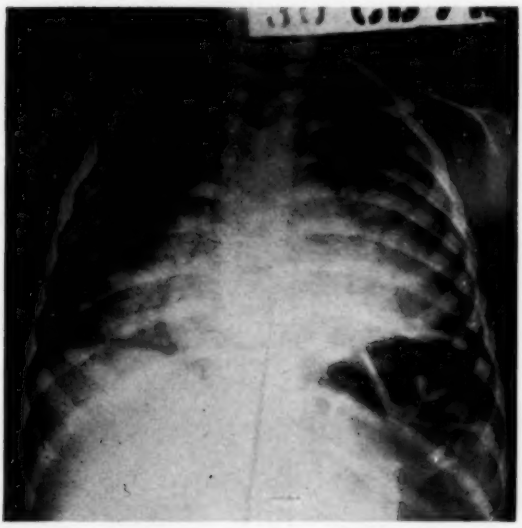

Fig. 3 (Case 2).—Roentgenogram of chest eighteen hours after kerosene ingestion; coarse mottled densities producing a lobarlike consolidation of both lower lobes.

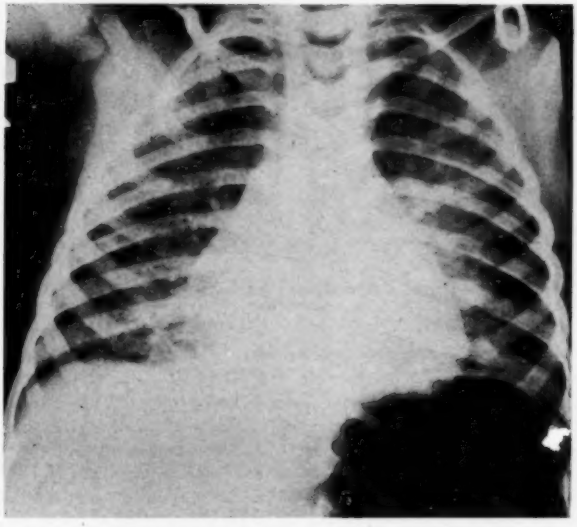

Fig. 4 (Case 2).—Forty-eight hours later. Resolution of the consolidation; both lung areas now have a mottled appearance.

CASE 2.—F. L. D., a 19-month-old colored male, was admitted to Grady Hospital with a complaint of unconsciousness and fever approximately twenty-four hours following the ingestion of an unknown quantity of kerosene. He was given an immediate dose of castor oil and lost consciousness soon afterwards. He was then brought to the emergency clinic, where gastric lavage was done. The examination on admission revealed a temperature of 101° F.; pulse, 104; and rapid, but not grunting respiration. He was fully conscious at time of admission. Examination of the lungs by two observers showed no abnormalities.

On roentgenologic examination, numerous coarse mottled densities appeared throughout the medial aspect of both lower lung fields, producing a somewhat pseudolobar consolidation (Fig. 3). Re-examination after forty-eight hours showed the consolidation in both lower lung fields to be less dense, and by then a fine mottled appearance was present (Fig. 4). The leucocyte count was 11,550 with an essentially normal differential. No urinary abnormalities were noted. A somewhat spiking fever, ranging from 100 to 103° F., subsided after about four and one-half days, and the child proceeded to an uneventful recovery.

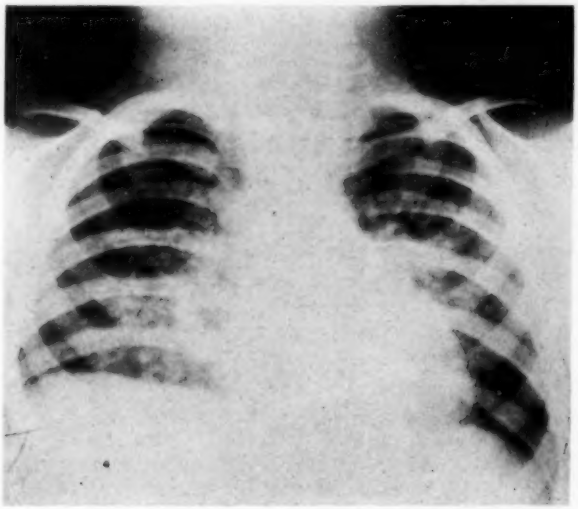

Fig. 5 (Case 3).—Numerous fine mottled densities in both hilar areas and the right lung base.

CASE 3.—D. T., a 15-month-old white male, drank an unknown quantity of kerosene seven hours before admission to the hospital. He was given magnesium sulfate shortly after ingestion. One hour later he appeared to have a fever and was coughing a great deal. Examination on admission showed a temperature of 103° F. The child was restless and fretful. The lungs were entirely clear to percussion and auscultation. A chest film on admission showed a fine haziness of the left intermediate and right lower lung fields. Numerous fine mottled densities were noted through both hilar areas and the right lung base (Fig. 5). A re-examination after three days revealed definite resolution of the process. There was still a fine haziness throughout both intermediate lung fields. The leucocyte count on admission was 10,050. The urine was normal. After several days of spiking fever, the patient made an uneventful recovery.

ROENTGENOLOGIC FINDINGS

X-ray examination of the chest was performed in twenty-two patients. The patients were not selected for this examination. During the last year, especially, all patients were studied roentgenologically regardless of clinical findings. Seventeen of these twenty-two patients developed pulmonary changes on x-ray examination. X-ray criteria of pulmonary involvement consisted of the appearance of fine or coarse mottled confluent or nonconfluent densities and diffuse densities in the lung fields. The presence of peribronchial reaction was not considered evidence of pulmonary involvement unless the above-described findings appeared on subsequent examination. This was observed on several occasions.

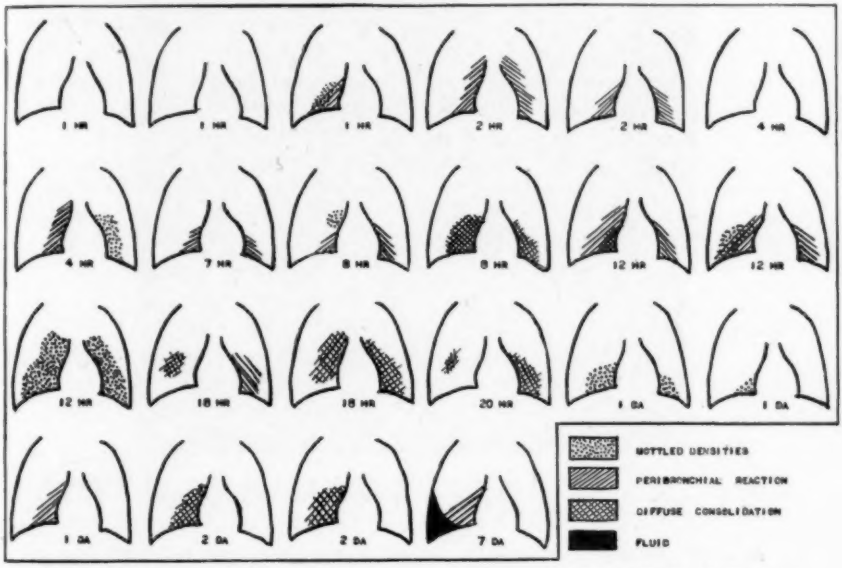

Fig. 6.—Diagrammatic representation of roentgenograms of the patients at the time of their first examination.

The roentgenologic appearance of the pulmonary manifestations are not uniform and may vary with the severity of the symptoms. In mild cases a patchy consolidation in the cardiophrenic angles is observed. This is usually preceded by a peribronchial reaction at the corresponding site. In more severe cases a diffuse density extends from both hilar areas toward the periphery of both lung fields. This opaque consolidation will resolve in the form of fine mottled densities. The pulmonary findings are seen early. Fig. 6 shows the x-ray findings of all patients at the time of the first x-ray examination. It will be noted that in two patients definite changes are present after one and two

hours and that most of the patients examined four hours after intake of kerosene showed definite roentgenologic findings.

AUTOPSY REPORT OF A CHILD WHO DIED AFTER KEROSENE INGESTION

S. J. W., an 18-month-old colored female who accidentally drank about 150 c.c. of kerosene, was immediately brought to the emergency room and admitted to the hospital. Physical examination revealed a well-developed, drowsy, colored female of stated age with a temperature of 103° F., a rapid, regular pulse (150), and a respiratory rate of fifty per minute. Numerous rhonchi and râles were present in all lung fields. These findings were interpreted as being due to pulmonary edema. Death occurred four hours after admission to the hospital.

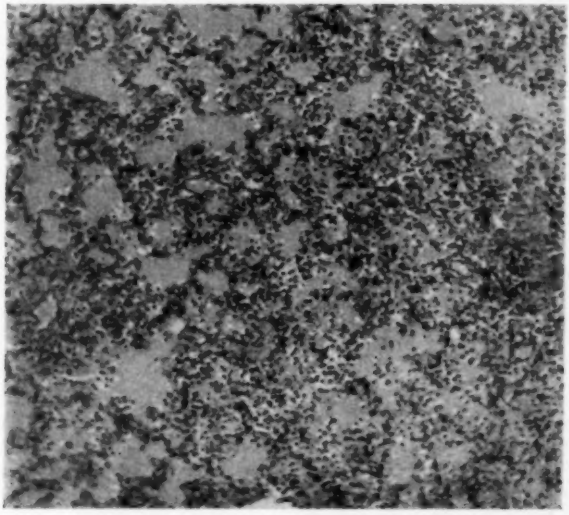

Fig. 7.—Section from the lung of an 18-month-old child who died four hours after kerosene ingestion. Note edema fluid in alveoli containing inflammatory cells and congestion of alveolar capillaries.

Essential Autopsy Findings.—On inspection the gastrointestinal tract had a normal appearance. The thymus was somewhat enlarged and had a hemorrhagic appearance. The lungs stood up prominently and had a purplish red color involving all of the lobes. There was a diffuse increase in density of all lobes of both lungs. On cut section the lungs were dripping with a large amount of frothy material coming from the parenchyma. The liver and gall bladder had a normal appearance. The spleen showed no remarkable changes. The pancreas was soft and had a pink color. The adrenal glands did not demonstrate pathologic changes.

The stomach was distended with gas and contained 20 c.c. of thick yellow mucoid material. Throughout the entire length of the upper intestinal tract the odor of kerosene could be detected. The Peyer's patches were markedly enlarged and hyperemic. The genitourinary tract had a normal appearance.

Sections from the lungs revealed a marked amount of edematous fluid in the alveoli. This fluid contained a large number of neutrophiles. The capillaries of the alveolar walls were distended with red blood cells. There was very little air-containing tissue observed (Fig. 7).

Sections from the intestines revealed marked hyperplasia of the solitary follicles. Sections from the other organs did not reveal any unusual features.

Anatomic Diagnosis.—Acute bilateral pulmonary edema.

Microscopic Diagnosis.—Pulmonary edema and acute pneumonia.

Comment.—This case is an example of a rapid death following the ingestion of a relatively large quantity of kerosene. On autopsy the marked pulmonary edema was the most outstanding feature. In addition the lungs showed microscopic evidence of acute pneumonia, a fact which may be of importance in the subsequent handling of these patients.

ANIMAL EXPERIMENTS

The purpose of this study was to determine whether the pulmonary manifestations of kerosene poisoning were due to the effect of aspiration or whether they were the result of irritation of the lungs following excretion of the kerosene absorbed from the gastrointestinal tract.

TABLE I

EXPERIMENTAL DATA FROM RABBITS RECEIVING KEROSENE BY STOMACH TUBE

RABBIT	WEIGHT (GM.)	AMOUNT OF KEROSENE (C.C.)	X-RAY FINDINGS	OUTCOME	AUTOPSY FINDINGS
1	1,227	20	Normal lungs	Recovered	
2	1,477	35	Normal lungs	Died in four days	No definite lung changes
3	1,590	50	Normal lungs	Killed after four days	Lungs normal
4	1,272	50	Normal lungs	Killed after twenty-four hours	Lungs normal
5	1,227	40	Normal lungs	Recovered	
6	1,250	40	Normal lungs	Died in three days	Normal lungs, kerosene in gastrointestinal tract

Rabbits were selected as experimental animals principally because these animals do not vomit and hence the differentiation between aspiration and absorption could be made more clearly. Varying quantities of kerosene were injected by stomach tube into each of a group of six rabbits (Table I). The position of the tube in the stomach was established by fluoroscopic examination. The lungs of these rabbits were checked by x-ray examination before and at varying intervals of time after the administration. Two of the rabbits which received 20 and 25 c.c. of kerosene, respectively, recovered uneventfully with no evidence of pulmonary involvement by x-ray examination. Two rabbits which received 35 and 40 c.c. of kerosene, respectively, died. On autopsy neither of these rabbits showed pulmonary involvement. Two

TABLE II

EXPERIMENTAL DATA FROM RABBITS RECEIVING KEROSENE INTRATRACHEALLY

RABBIT	WEIGHT (GM.)	AMOUNT OF KEROSENE (C.C.)	X-RAY FINDINGS	OUTCOME	AUTOPSY FINDINGS
1	1,112	0.75	Three hours, bilateral coarse mottled consolidation	Died in ten hours	Intense pulmonary edema; pulmonary hemorrhage
2	1,555	1	One hour, negative; two days, consolidation, right intermediate lung field.	Recovered	
3	1,555	1.5	One hour, mottled consolidation, right lung base; two hours, same	Killed after two hours	Hemorrhage in right lower lobe; pulmonary edema
4	1,359	1	One hour questionable consolidation left lower lobe; two days, definite consolidation, left lower lobe	Recovered	
5	2,036	2	Post mortem bilateral diffuse densities, left lung field	Died in fifteen minutes	Marked hemorrhage and edema throughout both lungs
6	2,204	2	Thirty minutes, coarse mottled densities, left lower lobe; three hours, pseudolobar consolidation, left lower lobe; twelve hours, coarse mottled densities right base; pseudolobar consolidation, left lower lobe	Died after twenty hours	Same as above

rabbits which received 50 c.c. of kerosene each were killed after one and four days, respectively. The lungs of these rabbits did not show any evidence of pathologic changes. All of these animals passed from the rectum varying quantities of kerosene which produced marked irritation of the anus and external genitals. The animals which received the larger quantities of kerosene were markedly drowsy and refused food and water. One rabbit developed marked hematuria and albuminuria.

In a second group of six rabbits quantities of kerosene varying from 0.75 to 2 c.c. were injected intratracheally (Table II). This was ac-

complished by means of direct puncture of the trachea with a hypodermic needle. The lungs of these animals were examined roentgenologically at intervals of time varying from thirty minutes to three days after the experiment. All of these animals developed pulmonary

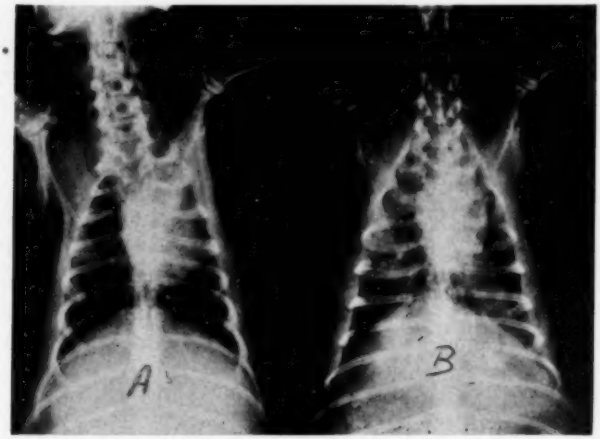

Fig. 8.—*A*, Roentgenogram of chest of rabbit before injection of kerosene. *B*, Same rabbit three hours after intratracheal injection of 0.75 c.c. of kerosene. Note confluent mottled densities in both lower lung fields.

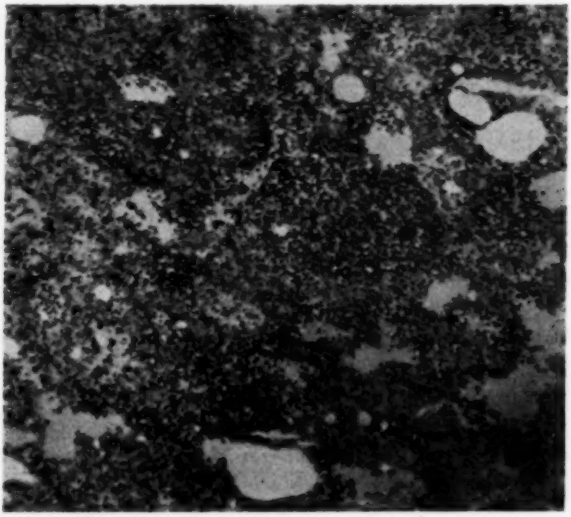

Fig. 9.—Section of lung from a rabbit which died ten hours after intratracheal injection of kerosene. Note intense pulmonary edema and large number of inflammatory cells.

manifestations characterized by more or less confluent densities, predominantly in the lower lung fields (Fig. 8, *A* and *B*). (All animals were injected intratracheally while in the upright position.) These findings were evident in most animals after an interval of from thirty minutes to one hour. In the two animals which recovered the areas of consolidation were more extensive on the second day; and in one animal which died after twenty hours, the pulmonary process had shown marked spread after twelve hours. The lungs of those animals which died or were killed showed rather remarkable pulmonary changes. On gross pathologic examination a marked amount of frothy blood-tinged fluid was noted in the trachea and in the large and small bronchi. On section of the lungs a large amount of edematous fluid escaped from the surface of the parenchyma. Grossly, there were interspersed throughout pinkish lung tissue areas which had a dark red appearance. These areas varied in size from a few millimeters to 2 cm. in diameter. They were not infrequently confluent, giving the lungs a grossly mottled appearance. On microscopic examination intense hemorrhage into the alveoli was found in the areas which had a dark red appearance. In those alveoli which showed fewer red blood cells a marked amount of pinkish staining edematous fluid was seen (Fig. 9). It was noted that this fluid contained a large number of inflammatory cells in sections from those animals which died after an interval of from ten to twenty hours. The presence of laryngeal edema was ruled out by careful dissection of the upper respiratory tract.

COMMENT

Although the number of animals used is not large, the evidence seems sufficient to state that in rabbits pulmonary manifestations associated with kerosene intoxication follow aspiration into the respiratory tract and not absorption from the gastrointestinal tract. The pulmonary lesions become evident shortly after aspiration and consist of areas of pulmonary edema and hemorrhage into the lung parenchyma. These areas correspond to those seen roentgenologically as coarse mottled densities.

DISCUSSION

From the above observations it can be stated that pulmonary manifestations as a complication of kerosene poisoning are present much more frequently than previously supposed. The physical findings in the chest are by no means adequate criteria for the diagnosis, especially in the milder cases, since we have repeatedly observed patients who showed very marked changes roentgenologically in the absence of physical findings. In previous reports it is stated that pulmonary complications in kerosene poisoning occurred in 39.1 per cent[3] and in 43 per cent[4] of the patients. These figures apparently were not based on routine roentgenologic studies. In the present group of patients studied roent-

genologically, whether or not physical signs were present, the incidence was 77 per cent.

Pulmonary manifestations developed with remarkable rapidity. This was a uniform finding in those children who came to early observation and roentgenologic examination. An identical observation was made in the animal experiments. One of the rabbits showed definite pulmonary changes in less than thirty minutes.

The pathologic findings seen in the reported autopsy and those seen in the experimental animals show a remarkable degree of similarity. Confluent mottled densities observed on radiologic examination correspond to areas of pulmonary edema and hemorrhage. Inflammatory changes indicated by the appearance of neutrophiles are observed early. This is demonstrated in the autopsied case and also in the sections of the lungs of those rabbits who died after an interval of several hours.

The statements that small hemorrhages and pulmonary congestion[2] and that local irritation and diffuse pneumonia[5] are observed after absorption of kerosene from the gastrointestinal tract are not borne out by our experimental studies. None of the rabbits which received kerosene by stomach tube developed pulmonary changes. The rapidity of development of pulmonary manifestations would also support the conception that they are the result of aspiration rather than absorption from the gastrointestinal tract.

The children observed in this group commonly demonstrated coughing or vomiting or both. The informants frequently stated that the children were seen to gag, and this gagging or coughing may well explain the mechanism of aspiration of the kerosene. Similarly, gastric lavage, commonly practiced as a therapeutic procedure in these cases, may provoke aspiration. For this reason it is probably advisable, unless the amount of kerosene ingested is very large, not to employ gastric lavage.

It is our feeling that chemotherapy alters very little the clinical course of the disease unless complicated by bacterial invasion. However, it may be advisable to employ these drugs prophylactically to avoid this complication.

SUMMARY AND CONCLUSIONS

1. Clinical and roentgenologic studies on a group of patients with kerosene poisoning, observed at Grady Hospital over a two-year period, are described.

2. Pulmonary manifestations were observed in 77 per cent of the patients examined roentgenologically, as compared with only 24.2 per cent found by physical findings alone.

3. These pulmonary changes are believed to be pulmonary edema, hemorrhage, and inflammation, as shown in animal experiments and an autopsy report.

4. It is believed that the pulmonary changes are brought about by aspiration of kerosene into the respiratory tract and are not the result of absorption from the gastrointestinal tract with subsequent excretion into the lungs.

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ACUTE INFECTIOUS MYELITIS FOLLOWING RUBELLA

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THE epidemic of rubella among the civilian and military population in the past year has emphasized the clinical importance of a contagious disease which in the past had been considered innocuous.

Encephalitis, myelo-encephalitis, and neuritis are described in the literature as occurring occasionally after upper respiratory infections, following measles, scarlet fever; also, with vaccinia.

Fox[6] reviews in detail four cases of acute infectious neuronitis or acute benign infectious myelitis following simple upper respiratory infections. He also reviews the literature, presenting 126 cases of a similar nature, recording their clinical findings and mortality figures. Ferraro and Scheffer[5] have presented an exhaustive and complete description of encephalitis and encephalomyelitis following measles. Sprott,[2] reports cases of eight patients with rubella with complications, four of whom showed arthritic symptoms and four, mild neuritic disturbances, and remarks: "in the remarkable change of a disease which has been remarkedly free from complications." Welch[3] reports a case of rubella with meningo-encephalitic symptoms.

In the 1937 edition of Price's *Text Book of the Practice of Medicine*, in the section written by Doctor Box, it is stated that "complications and sequelae in rubella are for all practical purposes nonexistent." Among the trivial complications that occasionally occur are mentioned rheumatic pains of a mild type, while encephalomyelitis is given as rare. He states, "A few cases of encephalitis and encephalomyelitis have been reported in France, but I have seen nothing of this kind."

Merrit and Koskoff[1] report four cases of severe neurologic disturbances following rubella and review seven cases from the literature. They also quote Sevestre as reporting the case of a young woman with delirium during an attack of German measles, Alliot as mentioning stiffness of the neck and conjugate deviation of the eyes in one case, and Labougle as reporting the case of a soldier with fever, violent headache, semi-coma, and athetoid movements with recovery. Siegel states that Freud and Pie cite several cases of hemiplegia after German measles in their monograph on infantile hemiplegia.

There have been reported in the literature, as reviewed by Read,[4] eighteen cases of encephalitis following German measles to May, 1936, with a mortality of 11.1 per cent.

The occurrence of the syndrome of acute infectious myelitis, or as also called, acute infectious neuronitis (benign), after rubella is uncommon and emphasizes the protean aspects of German measles on the central or peripheral nervous system.

We wish to report the following case of acute benign infectious myelitis with the clinical course and the essential laboratory findings:

P. M., 18 years of age, was admitted to St. Joseph Hospital, Far Rockaway, complaining of inability to walk. The patient had had rubella two weeks previously. He remained in bed four days. He felt well, returned to school, played baseball, and had no complaints. Two weeks from the onset of rubella, he noticed he was "weak in the knees." The following morning he was unable to walk and could not pass his urine.

Physical examination showed a well-nourished adult male appearing acutely ill. There was evidence of bilateral cervical lymphadenopathy. A fine brownish desquamation was present over the skin. Heart was normal; blood pressure, 120/70; chest, clear; abdomen revealed a large globular mass in the suprapubic region corresponding to the position of the bladder, which was sensitive to pressure.

There was an absence of the abdominal and cremasteric reflexes. The knee and Achilles jerks were markedly accentuated. There was no spasticity, flaccidity, or wasting. No Brudzinski or Kernig's sign was elicited. There were no pathologic reflexes.

The sensations of touch and pressure were present but exaggerated in both lower extremities. Thermal sensation was normal. There was no analgesia.

Laboratory Findings.—X-ray examination of the dorsal and lumbosacral spine showed no abnormality in the bones. *Blood count on admission:* hemoglobin, 84.5 per cent; red blood cells, 4,510,000; white blood cells, 17,600; polymorphonuclears, 92 per cent; lymphocytes, 6 per cent; monocytes, 2 per cent. *Urine on admission:* color, amber; reaction, acid; albumin, negative; sugar, negative; acetone, negative; micro: white blood cells average 1 h. p. f., red blood cells average 2 to 3 h. p. f. and few squamous epithelial cells. *Spinal fluid:* Cell count, white blood cells, 22 per cubic millimeter, all lymphocytes; smear, no organisms; albumin, 1 plus; globulin, trace; sugar, 90.3 mg.; chlorides, 728 mg. *Spinal fluid colloidal gold* showed no reduction. *Spinal uid culture* showed *Bacillus subtilis* (contamination). *Spinal fluid, April 26, 1943:* Albumin, 2 plus; globulin, trace; total proteins, 62.5 mg. per 100 c.c.

Eye Consulation by Dr. B. Esterman.—All extraocular muscles normal (III, IV, VI); pupils reacted to light and accommodation; no exopthalmus; media clear; ocular tension normal; discs not elevated, conjested, or hyperemic; retinal vessels of normal caliber.

Course at Hospital.—Temperature on admission, 103° F.; remained elevated for three days, returned to normal and remained so for the duration of the patient's stay in the hospital.

Urinary retention requiring catherization at intervals persisted for one week.

The patient's inability to walk without losing his balance gradually diminished from about the eighth day, and on leaving the hospital two weeks from the time of admission, he could walk if supported by an attendant.

The paresthesias markedly diminished so that on discharge they had almost disappeared.

The patella and Achilles reflexes returned to normal.

The cremasteric and abdominal reflexes were still absent.

Four weeks later all the above symptomatology had disappeared with the exception of the deep reflexes which were still absent.

DISCUSSION

While encephalitis and myelo-encephalitis have been occasionally described as occurring in rubella, the syndrome of acute infectious neuronitis or acute benign myelitis is practically unrecorded.

The ataxia, urinary retention, and paresthesias are due to degenerative (often inflammatory) process in any part of the peripheral neuron.

The above symptomatology, together with the acellular hyperalbuminosis of the cerebrospinal fluid, closely resembles the syndrome.

There are present three main views in the cause of this disturbance:

1. That the lesion in the cord is directly due to the action of the virus (Gorter and van Nederveen).

2. That they represent an allergic or anaphylactic phenomenon occasioned by the preceding illness (Rivers).

3. That they are caused by an unknown virus or toxin which is in some way empowered by the exanthematous disease to attack the nervous system (Levaditi, Nicolau, and Sanchez-Bayarri).

SUMMARY

1. The literature on the neurologic complications of rubella is reviewed.

2. The infrequency of the occurrence of acute infectious neuronitis or acute infectious myelitis (benign) in the literature is noted.

3. Rubella may be accompanied by many diverse manifestations of a widespread nature in the central nervous system, the above case representing the localization of the pathologic process on the nerve cell, nerve root, or peripheral nerve process.

4. Rubella per se is a relatively "simple" disease, but its neurologic complications require further study and interpretation.

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The Pediatrician and the War

The following is a continuation list of Fellows of the American Academy of Pediatrics on active duty in the military services:

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Special

Dr. Irving J. Wolman, Philadelphia, Pa. (U. S. Public Health Service)

News and Notes

The following have been admitted to membership in the American Academy of Pediatrics, Region V.

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Carlos Andrade Marín, Calle Pichincha 32, Quito

Venezuela

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Ernesto Vizcarrondo, Avenida Bogotá-Urbanización Los Caobos frente a la Quinta Ojai, Caracas

Peru

Enrique Leon García, Faculty of Medicine, Lima
Luis A. Suares, Insituto Nacional del Nino, Medical Division, Lima
Felipe Chueca, President of the Society of Pediatrics, Lima
Manuel Salcedo, Gallos No. 234, Lima
Horacio Cachay, Department of Pediatrics, Faculty of Medicine, Lima
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Noé Huamán, Instituo Nacional del Niño, Lima
Guillermo Filomeno, Instituo del Niño, Lima
Carlos Krumdieck, Washington 914, Lima

The Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals report the following recommendation:

"The wisest course is to postpone elective operations on the nose and throat during epidemics of poliomyelitis."

Submitted by,

JOHN A. TOOMEY, Chairman
E. J. HUENEKENS
CHARLES F. MCKHANN
WILLIAM BOYD READING
BELA SCHICK
HULDAH E. THELANDER

Book Review

Your First Baby. Modern Methods of Care and Feeding with a Personalized Baby Record Book. Louise Cripps Glimser, New York, 1943, A. S. Barnes & Co., 90 pages. Price, $1.

An attractive paper-bound book with brief and to-the-point discussions of the care of the baby. The material is more concerned with attitudes than specific details and follows modern thought in feeding, habit formation, and developmental considerations. The advice is good, simple, and clear. There are a number of full-page pictures of photogenic babies, which add nothing to the text, but which undoubtedly will appeal to the young mother. The last twenty pages are for a record of the baby's birth and development.